Exhibit A

REDACTED

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	)	MDL NO. 2875
	)	HON. ROBERT B. KUGLER
THIS DOCUMENT RELATES TO ALL CASES	)	

CONFIDENTIAL INFORMATION - SUBJECT TO PROTECTIVE ORDER

VIDEOTAPED DEPOSITION OF:
MICHAEL BOTTORFF, PHARM.D.
Taken on behalf of the Plaintiffs
March 25, 2022

REMOTE APPEARANCES:
For the Plaintiffs:
C. BRETT VAUGHN, ESQ.
Hollis Law Firm
8101 College Boulevard
Suite 260
Overland Park, Kansas 66210
For the Defendants, Teva Pharmaceutical Industries, Ltd., Teva Pharmaceuticals SA, Inc., Actavis LLC, and Actavis Pharma, Inc.:
STEPHEN T. FOWLER, ESQ.
Greenberg Traurig, LLP
2101 L Street, N.W.
Suite 1000
Washington, D.C. 20037
202.331.3100
Fowlerst@gtlaw.com

Also Present Remotely:

Alice Springer
Bailey Hughes
Christine Gannon
Daniela Tenjidor
Geoffrey Coan
George Williamson
Gerond Lawrence
Iris Simpson
Ken Dzikowski
Marlene J. Goldenberg
Melissa Catello
Melisha Valenzuela
William Murtha
Phillip Todd - Videographer

I N D E X

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The videotaped deposition of MICHAEL BOTTORFF, PHARM.D., was taken by counsel for the Plaintiffs, on March 25, 2022, commencing at 9:39 a.m. Eastern, via remote proceedings, for all purposes under the Tennessee Rules of Civil Procedure.

The formalities as to notice, caption, certificate, et cetera, are not waived. All objections, except as to the form of the questions, are reserved to the hearing.

It is agreed that Carissa L. Boone, being a Notary Public and Court Reporter, may swear the witness, and that the reading and signing of the completed deposition by the witness are not waived.

* * *

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THE VIDEOGRAPHER: Good morning. We are now on the record. My name is Phillip Todd. I am the videographer for Golkow Litigation Services.

Today's date is March 25th, 2022, and the time is 9:39 a.m. Eastern.

This remote video deposition is being held in the matter of Valsartan, Losartan and Irbesartan Products Liability Litigation in the United States District Court, District of New Jersey.

The deponent is Dr. Michael Bottorff.

All parties in this deposition are appearing remotely and have agreed to the witness being sworn in remotely.

Due to the nature of remote reporting, please pause briefly before speaking to ensure all parties are heard completely.

Counsel will be noted on the stenographic record.

The court reporter, Carissa Boone, will now swear in the witness.

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MICHAEL BOTTORFF, PHARM.D. having been first duly sworn, was examined and testified as follows:

THE VIDEOGRAPHER: I'm sorry, I did not hear anything from the witness.

I'm sorry, I did not hear anything from the witness.

THE WITNESS: I said "I do."

EXAMINATION

BY MR. VAUGHN:

Q. All right, Dr. Bottorff. My name is Brett Vaughn. You remember I took your deposition about six months ago in the general causation stage of the personal injury cases, correct?

A. I do remember you, yes.

Q. And you've now submitted an expert report for the class action side of this litigation?

A. Correct.

Q. And did you use your general causation expert report as the base of your class action expert report?

A. There was some overlap in what seemed to be some of the issues between the class

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action and the general causation, so there were some elements that are similar in both.

Q. And is this meant to supercede your general causation expert report?

MR. FOWLER: Objection, form.

THE WITNESS: Not to supercede. As -- as part of my academic career, whenever there's a -- a literature search and evaluation, a -- a process that you go through, you review and add information to what you already know. So it's not meant to replace previous information, if that's what the question was.

BY MR. VAUGHN:

Q. And so what content did you add to this expert report?

A. I think the biggest addition is the bioequivalence description assessment and analysis and a section on the process of pharmacokinetic accumulation. And then a -- a third area was a -- a section where I comment on the -- the need for medical monitoring.

Q. And you said that the purpose of this was not to replace previous information.

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Were there changes actually made, though, to your general causation opinions in here?
MR. FOWLER: Objection, form.
THE WITNESS: I don't recall making any changes to my previous report in this report.
MR. VAUGHN: Melisha, can we go ahead and pull up the class action expert report he submitted?
And that will be Exhibit 1.
(Exhibit 1 was marked.)
BY MR. VAUGHN:
Q. And, Mr. Bottorff, is this your -- the expert report you submitted for the class action in this litigation?
A. Yes, it is.
MR. VAUGHN: And, Melisha, can we split-screen that with his general causation report?
And let's mark that as Exhibit 2.
(Exhibit 2 was marked.)
BY MR. VAUGHN:
Q. Now, turning --
MR. VAUGHN: On the class action expert report, can we please go to page

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7, Melisha? And on the general causation report, can we go to page 6.
BY MR. VAUGHN:
Q. Okay. So on the right-hand side, you see on your general causation report, you -- line 114, that entire paragraph, you note: "When ZHP became aware of the nitrosamine impurities, ZHP tested certain of its inactive ingredient -- active pharmaceutical ingredient batches and determined that the levels of NDMA range from 3.4 parts per million to 120 parts per million"?
Do you see that, Dr. Bottorff?
A. Yes. Is that what you highlighted in yellow?
Q. Correct.
And then it -- looking at your class action expert report page 7, line 140, you see that it's now been changed to the FDA testing and any mention of ZHP's testing has been dropped from your export report?
MR. FOWLER: Objection to form, "changed."
Go ahead, Doctor.
THE WITNESS: I see where you're

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highlighting in blue. Or now yellow.
BY MR. VAUGHN:
Q. Do you have your class action expert report with you?
A. Yes.
Q. Can you find anywhere in your class action expert report where -- where it still discusses ZHP's internal nitrosamine testing on their API?
A. Yeah, I don't -- I don't see it.
Q. Are you the one that removed that from your expert report?
A. I probably was, since I wrote this myself.
Q. Why did you remove that from your expert report?
MR. FOWLER: Objection to form, "remove."
Go ahead, Doctor.
THE WITNESS: I can't tell you right now why I did not include the same wording. The -- the following information, which is the -- the FDA values, I believe they are identical.
BY MR. VAUGHN:

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Q. But ZHP's values are higher than the FDA's values, aren't they?
MR. FOWLER: Objection.
THE WITNESS: If I went back and calculated. (Technical interference) probably do that. But I think --
BY MR. VAUGHN:
Q. But --
A. -- they are higher.
MR. VAUGHN: All right. Melisha, can we go to page 22 on the class action report now? And let's compare that to page 21 of the general causation report.
All right. And I'm looking at line 364 where it says: "Presence of trace amounts of NDMA/NDEA on the general causation report," Melisha. The one on the right. Line 364. Yeah.
BY MR. VAUGHN:
Q. And then -- you see that, Doctor, line 364, where you note the -- the amounts being trace amounts?
A. Yes.
Q. Okay. And can we compare that, then, to your class action expert report on page

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22, line 374? It now says: "Presence of NDMA and NDEA," the words "trace amounts" have been dropped from your expert report, correct?
A. They're not there.
Q. Are you the one that removed those words?
A. I wrote this, so I must have.
Q. Why did you remove those words from your expert report?
A. I have no particular reason.
MR. VAUGHN: All right. Melisha, let's go to page 45 of this class action expert report. And let's compare that to page 25 of his general causation expert report.
BY MR. VAUGHN:
Q. In the general causation expert report on that line 439, the sentence that reads: "The concern over the detection of these impurities is that the international agency for research on cancer, IARC, has categorized nitrosamines as a probable human carcinogen based on annual studies primarily involving rats."
Do you see that in your general causation report, Mr. Bottorff?

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A. I do.
Q. Okay. Now looking at your class action expert report line 724, that entire sentence is no longer in your expert report, is it?
A. No.
Q. And did you remove that language from your expert report as well?
A. It's not there, so it got removed. But it wasn't removed for any particular reason that I can give you.
Q. And you're the one that removed that language?
A. I wrote this, so it would have been me.
Q. And there's no particular reason you removed the language about nitrosamines being probable human carcinogens?
MR. FOWLER: Objection, form. Other than the scope of the report?
THE WITNESS: And so, no, I -- I'm -- I'm the one, if it came out, that took it out. And there was no particular reason for that.

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MR. VAUGHN: Let's go to page 47 of his class action report, and let's compare that to page 27 of his general causation expert report.
BY MR. VAUGHN:
Q. And on your general causation expert report, I'm looking at the lines 473 and 474. So it ends with: "The carcinogens produced" at 473.
Do you see where I'm looking at, Mr. Bottorff?
A. Yes.
Q. And so now if you look at the class action expert report Line No. 749, you've now inserted a heading "NDE" -- "NDMA and NDEA and valsartan will not reach systemic circulation."
Do you see that, Dr. Bottorff?
A. I do.
Q. Why was that added to your expert report?
MR. FOWLER: Objection to form, "added."
THE WITNESS: I guess I was trying to -- doing what I would call sort of format form, outline form, sort

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of identify areas in this second report that I would have sections on. So it was a -- working from an outline to the report.
BY MR. VAUGHN:
Q. And does NDMA or NDEA reaching systemic circulation have anything to do with bioequivalency studies?
A. The presence of NDMA and NDEA in valsartan, are you asking if that would have an effect on valsartan's bioequivalence?
Q. Correct. Does NDMA or NDEA being in valsartan and the NDMA or NDEA reaching systemic circulation, does that have any impact on valsartan bioequivalency studies?
MR. FOWLER: Objection: Form, compound.
THE WITNESS: First, I'm -- I'm trying to speak real loud to make sure that you can hear. So if it seems like I'm yelling, it's not in an -- an aggressive kind of response.
BY MR. VAUGHN:
Q. I appreciate it and your -- your level is actually pretty good.

A. Okay. I -- I just didn't want it to come across as -- but I wanted to be sure I got heard.

No, I do not believe that the presence of NDMA or NDEA in valsartan has anything to do with valsartan's bioequivalence.

Q. And it reaching systemic circulation -- scratch that.

And NDMA or NDEA reaching systemic circulation has nothing to do with the bioequivalency studies for valsartan, correct?

MR. FOWLER: Objection: Form, lack of foundation, facts not in evidence.

THE WITNESS: Because I conclude that they would not reach the systemic circulation, then, again, my best answer to your question is that they have no effect on valsartan's bioequivalence.

BY MR. VAUGHN:

Q. The opinion that NDMA and NDEA in valsartan will not reach systemic circulation is in relation to your general causation opinions, correct?

MR. FOWLER: Objection: Form,

mischaracterizes.

THE WITNESS: I think it's, as I said earlier, that there is some overlap in some of the issues between general causation and this part of the litigation, as I understood it, and the concept of -- of first pass metabolism is one of those areas of overlap between the two reports.

BY MR. VAUGHN:

Q. How does first pass metabolism of NDMA or NDEA impact the bioequivalency studies of valsartan?

A. It does not.

MR. VAUGHN: Melisha, let's go to page 48 of his class action expert report. Let's compare that to page 28 of his general causation expert report. Looking at line 486 of his general causation report where it says: "Minimizing exposure to other tissues and organs..."

BY MR. VAUGHN:

Q. And the full sentence reads: "Smaller oral doses are metabolized in the liver

almost completely, minimizing exposure to other tissues and organs."

Do you see that in your prior report, Dr. Bottorff?

A. I do.

Q. All right. And let's compare that to the sentence that starts on lines 761 of your class action expert report that reads: "Oral doses at the levels detected in generic valsartan at issue in this litigation are metabolized in the liver almost completely, preventing exposure to other tissues and organs."

Did I read that correctly, Dr. Bottorff?

A. Yes.

Q. What changes did you make in that sentence from your general causation expert report to your class action expert report?

A. I don't feel that I made any substantial changes at all.

Q. Okay. Do you see in the general causation report you used the word "minimizing exposure to other tissues and organs"? The word "minimizing"?

A. Yes.

Q. And do you see that that's been changed to the word "preventing"? It now says: "...preventing exposure to other tissues and organs."

Do you see that?

A. I do.

Q. Do you not think there's much of a difference between "minimizing" and "preventing"?

MR. FOWLER: Objection, argumentative.

THE WITNESS: Conceptually, what those two sentence [sic] were -- I think mean the same thing about -- because of first pass metabolism, that you minimize exposure, you prevent exposure, you minimize/eliminate risk, and I think they're -- they're just a reflection of the fact that I did not just simply cut and paste from my previous report into -- into this report. I -- I sat down and wrote it de novo with the same knowledge base and information.

BY MR. VAUGHN:

Q. And this sentence that you

changed has nothing to do with the bioequivalency studies, correct?

A. Correct.

MR. VAUGHN: Let's go to page 52 of his class action expert report, Melisha. And let's compare that to page 62 of his general causation expert report.

BY MR. VAUGHN:

Q. All right. In looking at the class action expert report, line 830, do you see where you note that: "DNA repair mechanisms in humans can be as much as ten times higher than rats"?

A. Yes.

Q. Okay. And looking at your general causation expert report, do you see that language anywhere?

A. Not in the page that -- that you have in front of me.

Q. Do -- do you have your general causation expert report?

A. I can probably get a hard copy because we have a printer here, but I don't have it sitting right in front of me.

Q. Okay. You can also download it from the exhibit share file, if you would like to.

All right. Dr. Bottorff, if you could, could you review your general expert report and see if anywhere in that report you gave the opinion that DNA repair mechanisms in humans can be as much as ten times higher than rats?

MR. VAUGHN: And let's go ahead and go off the record while he's reviewing this document.

THE VIDEOGRAPHER: The time is now 9:59 a.m. We are off the record.

(Brief recess observed.)

THE VIDEOGRAPHER: 10:06 a.m., we're back on the record.

BY MR. VAUGHN:

Q. All right. Dr. Bottorff, now that you've had time to review your general causation expert report, did you find anywhere within that report that you gave the opinion that DNA repair mechanisms in humans can be as much as ten times higher than rats?

A. No, I -- I didn't find it. And -- and what I was looking for and what I thought I had in there -- and it may still be in

there; I just didn't have enough time to find it -- is I thought I made a statement somewhere in the report that said that the metabolism of -- of NDMA in the liver was occurring in the organ that had the highest capacity to metabolize it.

And that -- that may be in there somewhere if I go line-by-line and try to find it. So I may not have quantified it in the original report, and I quantified it here from a statement made in -- in one of the PEG articles.

Q. Does quantifying the DNA repair mechanisms in humans compared to rats have anything to do with your class action opinions?

A. Yes.

Q. I'm sorry? I didn't hear that answer.

A. Sorry. Yes.

Q. What does it have to -- what does -- scratch that.

What do DNA repair mechanisms in humans have to do with your class action expert report?

A. The issue of medical monitoring.

Q. And how does that relate to medical monitoring?

A. Based on first pass metabolism and limiting exposure of NDMA and NDEA to the liver, which has the best capability for DNA repair mechanisms, would mean that there's no exposure enough to downstream organs to justify medical monitoring, based on these principles of both first pass metabolism and DNA repair.

Q. So would it be fair to say that the DNA repair mechanisms relate to your class action expert report because you don't believe that nitrosamines can increase the risk of cancer in humans?

MR. FOWLER: Objection, form.

THE WITNESS: Yes. And that's consistent with what I concluded in my original report, and it's a portion of what I continue to conclude in this expert report.

BY MR. VAUGHN:

Q. And so you would agree that's a general causation expert opinion, the DNA repair mechanisms in humans?

MR. FOWLER: Objection: Form, mischaracterizing.

THE WITNESS: I would agree that

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it has relevance to both the general causation issue in my original report and to the medical monitoring issue that I addressed in this report.
BY MR. VAUGHN:
Q. And when we went off the record for you to review your general causation expert report and Mr. Fowler went off the screen, did he discuss any part of your testimony with you?
A. No. None at all.
MR. VAUGHN: All right. Melisha, can we go just to his class action expert report, which is Exhibit 1. And let's go to page 50 and look at line 802.
BY MR. VAUGHN:
Q. Doctor, in this paragraph, you're discussing the half-life of NDMA, correct?
A. Correct.
Q. And in your opinion, what is the half-life of NDMA in humans?
A. It's estimated to be about 13 minutes.
Q. And what are you basing that estimation on?

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A. I'm using the clearance values from one of the Gombar papers.
Q. Did you find the Gombar paper to be reliable?
MR. FOWLER: Objection, form.
THE WITNESS: In some respects.
BY MR. VAUGHN:
Q. What is half-life?
A. The time it takes for a compound amount to be cut in half.
Q. What do you mean "cut in half"?
A. Drop by 50 percent.
Q. Is that after it's been ingested?
A. No. These diag- -- these numbers came from the intravenous data from Gombar, which is the part that I don't have any problem with at all.
Q. But the half-life is in relation to the substance being inside the body, correct?
A. And in this case, getting there by giving it IV.
Q. And so that would mean after 13 minutes, if no metabolism is taking place of the NDMA, half of it will have disappeared?
MR. FOWLER: Objection, form.

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THE WITNESS: It is as a result of metabolism, and to a certain degree, distribution after IV administration that would result in taking 13 minutes in the estimate in humans, and anywhere between 4 and 26 minutes in other animal species who received IV dosing, for that original concentration to be cut in half, and in that same amount of time, for that concentration to be cut in half.
BY MR. VAUGHN:
Q. So let me make sure I understand --
A. -- and approximately --
Q. I apologize.
A. Sorry, go ahead.
Q. I'm sorry if I cut you off --
MR. FOWLER: Let's not --
BY MR. VAUGHN:
Q. -- with the delay.
MR. FOWLER: -- do that. Yeah.
BY MR. VAUGHN:
Q. It -- it was not intentional.
A. Yeah, so I'll -- I'll finish, and

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then we can take that question.
So literally what it amounts to is whatever that original concentration is after you give it intravenously, the half-life -- let's take a round number of ten minutes. It would take ten minutes for that concentration to be cut in half. In ten more minutes, that would be cut in half. And by the time you got to five of those, you can't detect the drug anymore. So a general pharmacology rule is five half-lives and the drug is essentially completely gone.
Q. So did I understand you correctly that if NDMA is given intravenously to a human, it's going to take approximately 13 minutes for it to decrease by half?
A. An estimate from the Gombar data would predict that, if you were to give it IV.
Q. And do you agree with that estimate in Gombar?
A. I think it's actually a pretty good estimate.
Q. Would it matter how much of a dose is given IV? Will that impact the half-life at all?
A. It could.

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Q. How so?
A. If -- if a smaller dose is given that is in the range of what we call linear pharmacokinetics, you'll get a -- a half-life value. And if -- if it's a process that can be saturated and you give a multiple higher dose, then you would saturate elimination and you would get a measured longer half-life.
Q. And in the Gombar study where you drew this 13-minute half-life, was it saturated or not?
A. Gombar used his nonsaturated IV dose to calculate and then estimate what he thought it would be in humans.
Q. And so in a nonsaturated IV dose in humans, NDMA would take 13 minutes to reduce the amount in half?
A. That is an estimate from the Gombar data.
Q. Doctor, do you know how long it takes for the blood to do a full circulation in the human body?
A. Off the top of my head, I -- I don't. I know I used to know that. And sometimes you'll see that expressed as how many cycles per

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day or how man- -- how long it takes for one cycle. So I know that's available information, but I don't have it off the top of my head.
Q. Do you have an estimate, even?
A. I know blood volume is approximately 5 liters. Typical cardiac output is about 3 to 4 liters per minute. So it -- it shouldn't take long. Less than ten minutes, maybe 20 minutes. I can't verify that.
Q. I mean, if -- if cardiac output is around 4 liters and blood volume is around 5 liters, wouldn't you think that it goes all the way around the body in about a minute?
A. Yeah, I don't think that's the case, though.
Q. Okay. You think it might be less than 13 minutes, though?
A. I --
MR. FOWLER: Objection, we're -- we're -- calls for speculation. He's answered this.
THE WITNESS: I really don't know. I'd have to look it up, because it's been a while since I've had to use that information.

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BY MR. VAUGHN:
Q. If the blood can go all the way around the human body multiple times in 13 minutes, the NDMA would be crossing the liver multiple times, wouldn't it?
MR. FOWLER: Objection: Form, lack of foundation, facts not in evidence, incomplete hypothetical.
THE WITNESS: The -- the best answer I can give you in a conceptual is that when a drug is given IV, whether it's NDMA or, you know, a -- an FDA-approved drug, giving it in the IV route, it does eventually, if it is metabolized in the liver, pass through the liver as part of its route of elimination.
BY MR. VAUGHN:
Q. If the liver is able to fully metabolize NDMA and systemic circulation takes less than five minutes, you wouldn't expect the half-life to be 13 minutes, would you?
A. The issue that I have in being able to answer it to the best of my ability is that I'm not sure the first part of the question

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is accurate. I think I would need to establish how long it takes.
But remember the liver only gets part of -- of cardiac output. Part of cardiac output goes to other organs as well.
Q. All right. Sitting here today, though, you have no idea how long it actually takes for the blood to go around the human body, do you?
A. No. I -- I -- as of right now, I don't. I know the value if I were to -- to look it up, but I don't have it in front of me.
Q. And that's not something you've looked into in forming your opinions for either of your expert reports that you've submitted in this litigation, correct?
A. Correct. And -- and nor do I know the relevance that have any impact on my opinions anyway.
MR. VAUGHN: All right. Melisha, let's go to his invoices.
And this will be Exhibit 3. It is a composite exhibit of all of the invoices that were produced.
(Exhibit 3 was marked.)

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MR. VAUGHN: All right. Let's go to page 3.
BY MR. VAUGHN:
Q. All right. Doctor, and do you see that you submitted a bill for eight hours of deposition time on September 1st, 2021?
A. That should probably be November. So that's a typo.
Q. Why should that be November?
A. Based on the in- -- sorry?
Q. Why should that be November?
A. Oh, no. That -- is that the date that we did the previous deposition?
Q. Well, we actually did the previous deposition on September 16th, which you also billed for.
MR. VAUGHN: Melisha, if you want to go to page 5 on his invoices.
BY MR. VAUGHN:
Q. Now we have another bill for $4,000 for an eight-hour deposition on September 16th, 2021 also in Knoxville and the same start and end time.
A. Yes. I understand now what happened. I sent an invoice to GT for the date of

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the deposition, not knowing that that's not who should have received the invoice. So this invoice that I sent to GT was never paid.
The other invoice was sent to -- I don't know which law firm, but they are the one who eventually paid that invoice. So I was not paid twice for that deposition.
Q. Why is there a date inaccuracy of it being September 1st on page 3 of your invoice?
A. Because I'm not very good at sometimes having the correct date on there.
MR. VAUGHN: All right. Can we go to the next page, Melisha, page 4.
BY MR. VAUGHN:
Q. And on September 1st, on this bill, you also billed three-and-a-half hours for reviewing Lagana's deposition and conference call with counsel, correct?
A. Correct.
Q. Is that what you actually did then on September 1st instead of the deposition?
A. Yes, because we just previously established that that was not the date of the deposition.
Q. Okay. And then looking at

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September 16th, which was the date of the actual deposition, you also billed two-and-a-half hours for reviewing articles in advance of the deposition. So that's just the morning of the deposition you're billing?
A. Correct.
Q. Okay. And then the next one on October 6th, you note that you: "Preview/find Wang article for inclusion and articles considered."
What does that mean?
A. That I looked at those articles to see if I wanted to include them in my articles for consideration.
Q. That was after you submitted your expert report and after you sat for deposition, correct?
A. Correct.
MR. VAUGHN: Let's go to page 7, Melisha.
BY MR. VAUGHN:
Q. All right, Doctor. Is this where you started working actually on your class action expert report?
A. Correct.

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Q. And throughout this I note names Steve Fowler, Ken -- I'm not even going to try and pronounce that last name -- T. Harper. Are these all GT attorneys?
A. Yes.
Q. And is Greenberg Traurig, is that the law firm you were working with in generating this class action expert report?
A. Yes.
Q. Is that the only law firm that you were working with?
A. Yes.
Q. And you were providing opinions on bioequivalency studies of all of the Defendants in this litigation, correct?
A. Yes. All that I received information on.
Q. And GT, Greenberg Traurig, was the one responsible for giving you documents for each Defendant?
MR. FOWLER: Objection, form.
THE WITNESS: Yes.
Every -- every document from manufacturers on ANDAs and bioequivalence studies that I received,

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that came through GT. I did not deal with any of the companies directly.
BY MR. VAUGHN:
Q. Or any of the other law firms?
A. Or any other law firms.
Q. And so if there were additional documents that you wanted to review, Greenberg Traurig attorneys would have been who you went to?
A. Yes.
Q. Were there documents that you specifically asked to see, or is it just documents that Greenberg Traurig gave you?
A. I asked GT to send me, from as many of the manufacturers as they could, bioequivalence studies that were used to file and -- and received approval for their ANDAs. And -- and then it was out of my hands what I received at that point. It was up to the companies to find and send me those reports through GT.
Q. And so you would have expected that all of the bioequivalency studies were given to you, correct?
A. I don't expect that. I didn't know what I was going to get. I just evaluated

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what I did get.
Q. So I note typically on this you note that you're reviewing ANDA files for bioequivalency data. Why is it the ANDA files that you're reviewing to find the bioequivalency data?
A. It's -- the part of the ANDA submission process is to include the -- the BE data. So I would often get a file that had 50, 60, 70 folders in it, and I had to sift through those and find the ones that actually had the bioequivalence data in there.
So there's data on analytical, the case report forms on all the volunteers who were in the studies, what their lab values were, their physical exam results. I mean, there was a lot of information that's included, and it was just the BE data that I was interested in sifting through and finding.
Q. Each of those ANDAs are several thousands of pages, correct?
A. Correct.
Q. And when you said --
A. Just to add -- I'm sorry. Just to add and see if it helps. For some of the

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manufacturers, instead of several thousand pages, I only received the BE data only, and so I didn't have to sift through for some of the situations a lot more information than necessary for what I was doing.
Q. Do you recall for which companies that was?
A. Not off the top of my head, no.
Q. A second ago you testified that the submission process is to include the BE data. By that, do you mean that the company is supposed to submit all of their bioequivalency data and studies with their ANDA?
A. I believe that to be the case.
Q. And that's why you thought it was appropriate just to review the ANDA for their bioequivalency data, correct?
A. Well, or the bioequivalence data, if that's all they sent me. I -- it was the bioequivalence data that I was most interested in.
Q. And when you're talking about the data, did you actually review the underlying data or did you just review the final report?
A. It depends on the format that it came to me. There was often a lot of underlying

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data. There were bioequivalence data in humans. A lot of that had subject-by-subject what their individual values were. Then it had summary data on top of that. It just depended on the format in which I received it.
Q. And did you look into the testing methods that were employed in the different bioequivalency studies?
A. In some of the more extensive files that I received, there were testing data.
Q. And -- and for which manufacturers did you have the more extensive data?
A. Again, I'd have to go back and -- and look at my files to make that kind of accurate answer.
Q. Was it a majority or a minority of the Defendants that you had extensive data on?
A. I'd say it was about half. So when you look in my report to see which BE studies I included, I'd say about half of those came from looking at a lot of extensive information, and some were a little bit more targeted towards just the bioequivalence data.
MR. VAUGHN: Melisha, let's go to

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the first page of those invoices again.
BY MR. VAUGHN:
Q. And I just want to run through the billing amount, total billing amounts, Doctor. So this first invoice was $26,000, correct?
A. Correct.
MR. VAUGHN: And second invoice, Melisha, page 2.
BY MR. VAUGHN:
Q. This was $42,250, correct, Doctor?
A. Correct.
Q. And the third invoice was $4,000, correct?
A. Yes, but that may be the one that did not get paid because I sent it to the wrong firm for payment.
Q. And do you recall what firm you sent that to?
A. I sent it to GT, and they sent it to whatever firm was responsible for that.
Q. Then the next invoice is $35,500, correct?
A. Correct.

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Q. And the next invoice is $4,000?
A. Again, that may be the overlap with the other one. So both of those did not get paid. One did; one didn't.
Q. Okay. And the next invoice is for $5,000?
A. Correct.
Q. And the next invoice is for $41,000?
A. Correct.
Q. And your final invoice is for $46,084, correct?
A. Correct.
Q. And my math shows that all those together is $204,000. If we drop that other 4,000, we're at $200,000. Does that sound about correct to you, Doctor?
A. That sounds right.
Q. And have they paid all of those invoices to date?
A. Yes.
Q. And do you have additional time that you have not billed, that is not reflected in this billing?
A. No, I'm sorry. I'm sorry. The

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one you're on right now.
Q. Yeah, the last one?
A. I have not -- I have not been paid for that one.
Q. Okay. And then do you have outstanding time that you have not billed?
A. Yes. Between the end of last week and up until today, I've not billed for that.
Q. And approximately how much time is that?
A. Approximately, I'm going to say, 30 hours.
Q. And what were you doing during those 30 hours?
A. Reviewing my report, reviewing deposition transcripts of some of the Plaintiff experts in this phase of the litigation, rereviewing some of the articles that I thought were most important to my conclusions. I think that's the majority of the work.
Q. How many meetings have you had with counsel in preposit- -- preparation for this deposition?
A. We met yesterday here in Atlanta,

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and we had three remote sessions between the end of last week and the first part of this week.
Q. When you say "we," is that all Greenberg Traurig attorneys?
A. Yes.
Q. Approximately how many hours would you say those meetings were in total?
A. Maybe 16, 18 hours.
Q. And do you not charge Greenberg Traurig more money for when you take a deposition versus when you're just writing an expert report?
A. No, I don't charge differently.
Q. Let's go ahead and take a five, ten-minute break.
MR. VAUGHN: Is that okay, Steve?
MR. FOWLER: Five minutes would be good. But yeah, go ahead.
MR. VAUGHN: Sounds great. Can we get a breakout room?
THE VIDEOGRAPHER: Yes. The time is now 10:35 a.m. We're now off the record.
(Brief recess observed.)
THE VIDEOGRAPHER: The time is 10:43. We're back on the record.

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MR. VAUGHN: All right, Melisha, can we go back to Exhibit 1, Dr. Bottorff's class action expert report? And let's go to page 30.
BY MR. VAUGHN:
Q. And, Doctor, is this where you begin discussing these bioequivalency studies of the various Defendants?
A. Yes.
Q. All right. This first one that you note is for Teva valsartan, and it's ANDA 090642, correct?
A. Correct.
Q. And those studies, you note, were conducted in 2004, correct?
A. Correct.
Q. In your opinion, was Teva's valsartan contaminated with nitrosamines in 2004?
A. I don't believe so, but I don't know for sure.
Q. Is that something you asked counsel?
A. No.
Q. Is that something you looked into in any way at all?

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A. No.
Q. If Teva's valsartan in 2004 was not contaminated with nitrosamines, how does this study support that nitrosamines won't impact the bioequivalency of valsartan?
A. In this particular case, I was wanting to be thorough and include as many of the bioequivalence studies as I could get and not leave those out that -- for whatever reason or any other reason. So I asked for all of them. And every one of them that I got, I included in this report.
Q. In the body of your expert report, you included every single bioequivalency study that was provided to you by Greenberg Traurig?
A. That was provided to them by the companies who were requested to send it to me, yes.
Q. And so you would agree, though, that if, in 2004, Teva's valsartan was not contaminated with nitrosamines, this bioequivalency study does not tell you if nitrosamines will impact the bioequivalency of valsartan, correct?

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MR. FOWLER: Objection to form.
THE WITNESS: Again, I don't know if it was or wasn't, because I've -- I've not traced company documents about that kind of thing.
BY MR. VAUGHN:
Q. Right. I understand that you're -- you do not know, Dr. Bottorff, but if it's an "if-then" question. If it was not contaminated, then this would not tell you anything about if nitrosamines impact valsartan's bioequivalency, correct?
A. In and of itself, no.
Q. Going down to line 496, you have a sentence that reads: "The AUC and Cmax values are expressed as geometric means rather than the more common arithmetic means, since the pharmacokinetic data are usually more log-normal distributed, such that geometrics means giving more accurate description of the central tendency of the data."
Can you explain what that means to me, Dr. Bottorff?
A. I -- I can as much as neither you or I are not statisticians. But this is the

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common way in which all of these bioequivalence studies are conducted. It's expected in -- from the FDA when these are submitted that they're analyzed in that fashion. And it's done for the reason that I list here, which has to do with how the data are distributed across normal volunteers.
A lot of statistics are done assuming that a negative value could be the same as a positive value, which would lead to that normal distribution in statistics. But when you give a drug and measure AUC, it can only go up. It can't go down. So that's part of this unequal distribution that leads to this format of demonstrating the central tendency using the --the log-normal data.
I can describe how it's done, if you want to know.
Q. You're not a statistician, are you, Dr. Bottorff?
A. No, but I've had classes in statistics and I've actually taught classes in biostatistics.
Q. What is your prior experience with bioequivalency studies?
A. My first bioequivalence study

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experience was when I was a -- a -- a trainee in my residency at the University of Kentucky, and I worked in a unit that conducted these kind of bioequivalence studies. And I've done some of my own bioavailability studies where the conduct of the trial is essentially the same.

Q. What does geometrics mean? What does that mean?

A. Yeah. An arithmetic mean is you take -- let's say we are have three numbers, A, B, and C. You take A plus B plus C, and then you divide by three and that's the arithmetic means. The geometrics mean is you multiply A times B times C, and then you take the cube root of that number.

Q. And why does the geometric mean then give a more accurate description of the central tendency data?

A. Well, that's where it gets beyond my statistical understanding, other than it's what's expected to be done in these kind of studies, is they use the geometric instead of the arithmetic mean.

Q. Are you familiar with the term "harmonic mean"?

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A. Yes. There are -- there are multiple ways of -- of displaying central tendency. That's another one.

Q. What is a harmonic mean?

A. I've never used it, so I can't define it for you off the top of my head.

Q. What about a least squares mean?

A. That's really part of these as well, is because the FDA expects you, when you do a comparison from drug A to drug B, to not give everybody drug A first and drug B second. Some people will get drug B first and drug A second. And so you put that into a regression model along with the means, and the regression model that gives you the least difference, which is the least squares fit to the data, are how you determine the actual values that are going to be reported. So it's part of the regression model.

Q. What did you mean by "you put that into a regression model along with means and the regression model that gives you the least difference"? What do you mean by "the model that gives you the least difference"?

A. Yeah. The -- the best way I can describe it is if -- if you have average blood

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level versus time data that go sort of up and down, and you try to find the model that draws the best fit through that data, each data point that's not on that line -- as there's a difference between the point and the line that's calculated. And then the line is refit, the line is refit, and you take the square of that difference between the points in the line, and then you select the model that gives you the least squares difference between the predicted values and the observed values.

Q. Is there a difference between least square means and geometric least square means?

A. No. I think that's a different way of wording the same process that's done in bioequivalence studies.

Q. And what's going to give a more accurate description of the central tendency of data, a geometric mean or a geometric least squares mean?

A. It's the same thing.

Q. Oh, those are interchangeable as well?

A. Those -- those are

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interchangeable.

Q. Thank you.

MR. VAUGHN: All right. Let's go to page 31 of his expert report now. And looking down at the paragraph that starts on line 508.

BY MR. VAUGHN:

Q. I like that you line number your expert report, by the way. It makes it much easier to go through.

So this is the Princeton ANDA for the valsartan 320 milligram, ANDA 204821, correct, Doctor?

A. Correct.

Q. And the two studies that were done here, there was a fasting study, H237-11.

What is a fasting study?

A. Typically the FDA requires, when you do these studies, to do one study in -- where you dose in the morning after an overnight fast so there's no food in the stomach, and then you repeat the study with food in the stomach to -- like after a standard breakfast kind of meal to see if there's any effect of food altering the bioavailability or the bioequivalence.

Q. And you note that these studies were done in March and April of 2012. Did you look into the manufacturing date of the product that was actually tested in these bioequivalency studies?

A. I -- I didn't for a -- a point of record, but most of the files that I received, there was a section you could go to and it would talk about the date of actual production of what was going to be called the test product, and they even had the date of production of the -- of the reference Diovan. And they would even often have what the testing results on those individual products were.

You know, if it said it had 320 milligrams, did it have 320 or right around there? So those were often included in the records that I reviewed.

Q. Do you recall approximately how much earlier most of the manufacturing dates were than study dates? Several months?

A. A few months. These are usually batches that are not so large, because they want to prove that they can demonstrate bioequivalence with them before they go into more larger scale

production.

Q. Do any additional tests related to bioequivalency have to be done when a company scales up production?

A. I know there are times. The majority of these, the FDA requires the in-human bioequivalence study to be done on the largest tablet size that you're going to market. That's why these are almost always in the 320 milligram dosage. And then you're allowed to do in vitro dissolution testing with the smaller doses.

So even though the bioequivalence study might have been done with the 320, the ANDA got approved for 40, 80, 160, as well as the 320. And that was often done based on dissolution testing. So when you upscale, you can often demonstrate bioequivalence using the dissolution testing rather than repeat your human trial at that point.

Q. And do you know if Princeton's valsartan was contaminated prior to March of 2012?

A. I don't specifically know that.

Q. And, again, if Princeton's valsartan was not contaminated with nitrosamines at the time of this study, then this -- these

studies on bioequivalency don't tell you anything on if nitrosamines impact valsartan's bioequivalency, correct?

A. Not by itself.

Q. And what do you mean by "not by itself"?

A. Well, this report -- and I'm sure we're going to keep going through it -- is going to be leading to other bioequivalence studies with some of the combination products where I demonstrate that the addition into a valsartan tablet of milligram quantities of other compounds that do not have overlapping metabolic or distribution pathways do not also alter the bioequivalence. And so to me, it doesn't -- if it is or isn't in there, it's not going to alter the bioequivalence pattern.

Q. About line 513, you discuss Hetero Labs' ANDA 203311 and Studies 10-VIN -- V-I-N -- -337 and Study 330-VALS-2011, and you note that these studies were conducted in February and July of 2011, correct?

A. Correct.

Q. And do you know if Hetero Labs' valsartan was contaminated with nitrosamines in

2011?

A. Again, I don't. It -- it's my understanding that some of these generic manufacturers were making their drug with a process that may have had nitrosamines in it and they didn't know it. So I can't tell you with each company where that was and when that happened. I -- I'm somewhat certain that some of these did and it wasn't known, but it still didn't alter the bioequivalence.

Q. And so is it your testimony today that Hetero Labs' valsartan might have been contaminated with nitrosamines dating back to at least 2011?

A. It is my testimony that I don't know which companies may have had it, but that I'm suspicion [sic] -- my suspicion is that some did, and I don't know which.

Q. All right. Go to page 32, line 517. You are now discussing a Torrent Pharmaceuticals' ANDA 202728 with Studies PK-09-100 and Study PK-09-103. These are on valsartan 320 milligrams, and you note that the studies were done in July of 2010, correct?

A. Yes.

Q. And Torrent's valsartan, is it your opinion that it was contaminated with nitrosamines back in 2010?
A. It is my opinion that I don't know if it was or not.
Q. And if Torrent's valsartan was not contaminated with nitrosamines back in 2010, these bioequivalency studies don't tell you anything in relation to if nitrosamines impact the bioequivalency of valsartan, correct?
A. And, again, as I said before, not in and of themselves. But as we keep working through this, you'll see one of the premises about having combination products with more than valsartan, like hydrochlorothiazide in six-and-a-half -- or six-and-a-quarter up to 25 milligrams, amlodipine 5 or 10 milligrams, having no effect on the bioequivalence of -- of valsartan because of a lack of overlapping metabolic pathways.
And so as I've -- I've demonstrated in both reports, the lack of an overlapping metabolic pathway between the nitrosamines and valsartan, that there would be no reason, and in fact there couldn't be any reason,

to have that have any effect on the bioequivalence of valsartan.
Q. What were the two combination drugs that you just mentioned? Amlodipine and what was it?
A. Hydrochlorothiazide. Those are the components of the brand name Exforge or Exforge HCT.
Q. Are either of those drug genotoxic -- genotoxins?
A. No.
Q. Are nitrosamines genotoxins?
A. In animals, yes, depending on the exposure level.
Q. All right. On the PK-09-103 Study, on that far right-hand column, it says: "90 percent C.I."
What does the C.I. mean?
A. It's a confidence interval. The 90 percent confidence interval around that value in the column before it, which is the percentage similarity between the brand name and the test product. So it's a -- an -- the average value with the 90 percent confidence limits around that value. And these are to -- these confidence

limits are to demonstrate that they remained within the FDA guidelines of the confidence limits being allowed to be as low as 80 percent or as high as 125 percent.
Q. So does that mean that --
A. That would be for the A- -- I'm sorry. Whether that be for the AUC value or the Cmax value.
Q. And so does that mean that 10 percent of the population is allowed to fall outside of the 80 percent to 125 percent range?
A. No, that's not what it means.
Q. Can you explain further?
A. Sure. What it means is that if you were to redo this experiment 100 times, 90 times you would still get values that are between that range of upper and lower limit. So it's more of a statistical value than a what-happened-to-a-patient value.
Q. I understand now. I appreciate that clarification.
And so on the PK-09-103, it's getting up to 123.65 percent, and that's okay because it's less than 125, correct?
A. Correct. That's the upper limit

of the FDA's guidelines for demonstrating bioequivalence.
MR. VAUGHN: Let's go to page 33, Melisha.
BY MR. VAUGHN:
Q. All right. Line 537 and 538, you note that: "HCTZ" -- and what's HCTZ?
A. Hydrochlorothiazide.
Q. Is it okay if I refer to it as HCTZ in the deposition?
A. For me it is.
Q. Appreciate it.
You note that: "HCTZ is primarily eliminated through the kidney," correct?
A. Correct.
Q. And then you say: "Therefore, HCTZ would have no pharmacokinetic or pharmacodynamic overlap with valsartan or NDMA or NDEA," correct?
A. Correct.
Q. And why is that?
A. Well, there's multiple parts to that question. I previously demonstrated how valsartan is absorbed, taken up into the liver, excreted in bile and has a mild cytochrome P450

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pathway of elimination. None of those are shared by Hydrochlorothiazide. None of those are shared by NDMA or NDEA.

And I guess I should add that's the pharmacokinetic reason for no overlap. The pharmacodynamic reason is that -- that gets to their mechanism of action. How does Hydrochlorothiazide lower blood pressure? Not the same way that valsartan does. So there's no overlap between their -- their blood pressure effects. So that would be a lack of a pharmacodynamic-shared mechanism.

Q. And so is part of the reason that there's no overlap is they're being metabolized in different organs?

A. Well, that's part of it. Part of it can be you're metabolized in the same organ but by a different pathway. You would still then have no overlap.

Q. And NDMA is metabolized, in your opinion, in the liver, correct?

A. And how it's given and how much dose is -- is given.

Q. The NDMA that has been contaminated in valsartan, it's your opinion that

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it's metabolized in the liver, correct?

A. When ingested orally, yes.

Q. And valsartan itself is also metabolized in the liver, correct?

A. By a different metabolic pathway entirely.

Q. And is that the P450 pathway that you were just mentioning?

A. Well, there's a P450 pathway for NDMA that's separate and distinct from the minor P450 pathway with valsartan.

Q. But they're both metabolized through a P450 pathway, correct?

A. Correct, but a separate and distinct different P450 pathway.

Q. And then line 545 you note that: "Amlodipine is primarily hepatically metabolized."

And that means metabolized by the liver as well, correct?

A. Yes.

Q. And -- I'm --

A. Again, by a distinct metabolic pathway called 3A4.

Q. P450, 3A4?

A. Yes.

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Q. And is --

A. Different from valsartan, separate from NDMA.

Q. Thank you. You knew my next question.

Now, I don't see that you gave an opinion like you did with HCTZ that it would have no pharmakinetic [sic] or pharmadynamic [sic] overlap with valsartan or NDMA/NDEA.

Is that also your opinion, though, with amlodipine?

A. Yes. I -- I say the same thing in the next sentence, but in a slightly different way, because there's no identified mechanism of drug interaction or no overlapping route of metabolism.

Q. Can liver cirrhosis impact the metabolism of any of these drugs?

A. Not in a predictable fashion.

Q. What do you mean by that?

A. Well, there are probably maybe as many as 100 or 150 different cytochrome P450 pathways. Some of them have been studied for alterations in cirrhosis; some have not. Most do not show a change in their metabolic capability in

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cirrhosis.

Q. So liver damage could impact the metabolism of these drugs?

MR. FOWLER: Object to form.

THE WITNESS: It's probably been studied and there's other types of liver damage from cirrhosis, so it can't be yes/no. You have to look at the type of liver damage and the specific P450 pathway to see what's actually been demonstrated or shown not to have an effect. But it can't be done as a blanket statement.

BY MR. VAUGHN:

Q. Do you have an opinion as to what type of liver damage would impact the metabolism of any of these drugs the most?

MR. FOWLER: Objection: Form, foundation.

THE WITNESS: I don't. As I said before, it's not something you can say in a blanket yes/no format. So you'd have to literally look at each pathway and the multiple different types of hepatic disease to see what's been done

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and what's not been done.
MR. VAUGHN: Let's go to page 34, Melisha.
BY MR. VAUGHN:
Q. And at 559, we're now at the section on Exforge. What is Exforge?
A. That's the brand name of the combination product of valsartan and amlodipine made by Novartis.
Q. Okay. So when one of the companies is doing their bioequivalency studies on valsartan plus amlodipine, they do it in comparison to Exforge?
A. Correct.
Q. And line 562, you are now discussing Aurobindo's ANDA 206512, and within that, their Study No. 368-12 and 369-12. And you note that these were done in October of 2013, correct?
A. Correct.
Q. And you don't recall the date of manufacture of the generic pills that were being tested, do you?
A. No. Again, they would have been within some, usually few months time frame, but I

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don't know.
Q. Okay. So is it your opinion that Aurobindo's valsartan was contaminated with nitrosamines prior to October of 2013?
A. It is my testimony that I do not know, but that it may have had. And that if it did, it didn't alter the bioequivalence anyway.
Q. And if it -- if that -- scratch that.
And if Aurobindo's valsartan was not contaminated with nitrosamines during this time, then these bioequivalency studies don't tell you anything as to if nitrosamines will impact the bioequivalency of valsartan plus amlodipine, correct?
A. Well, no, not necessarily correct. Because, again, in microgram quantities, without any overlapping mechanism for an interaction, there's no reason to expect that there would be any impact at all.
Q. But if this study is testing pills without any nitrosamines in it, how does that add anything? How does that support your opinion that the nitrosamines aren't going to impact the bioequivalency?

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A. Again, it -- it can't. There's no mechanism for it to do such. This, again, study in and of itself is demonstrating that by showing that you still get all the valsartan you're supposed to get, even when amlodipine is present, because it doesn't share a metabolic pathway.
Q. Did you even need to look at any of these bioequivalency studies, as you had already determined that there's no way that nitrosamines can impact the bioequivalency of the drugs?
A. Well, the -- the process that I went through was not starting with that. I first had to go through the metabolic pathways of these various components and then look at the bioequivalence studies and then draw my conclusion at the end of that, not on the front end of that.
Q. And you think that studies done without nitrosamines can tell you if nitrosamines are going to impact the bioequivalency?
MR. FOWLER: Objection: Form, mischaracterizes.
THE WITNESS: Again, I think in answering that previously, I -- I said

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that not in and of themselves. You have to look at the whole picture. And part of the whole picture is valsartan's bioequivalence is retained in the presence of other compounds, that I had to see the data for, before I could draw that conclusion.
And then also understanding that some of these probably had nitrates in them, even as far back as -- as when these bioequivalence studies were done.
BY MR. VAUGHN:
Q. You just testified that you have to look at the whole picture. What do you mean by "the whole picture"?
A. Look at all the compounds involved, their metabolic pathways, the bioequivalence studies.
Q. All of the bioequivalency studies?
A. All that I received, which supported my contention and the -- all of the metabolic pathways of all the compounds involved.
Q. If there were other bioequivalency studies that you did not receive,

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you wouldn't have the whole picture, would you?
A. I wouldn't have any more information than what I've already put in my report, but I think there's adequate information in my report to make my conclusions.
Q. If there were bioequivalency studies that -- scratch that.
If some of the generic manufacturers conducted bioequivalency studies on their valsartan and they failed the bioequivalency studies, you would then ex- -- you would have expected the Defense attorneys would have given you that information, correct?
A. And they did.
Q. How do you know they did?
A. I saw one bioequivalence study that the average AUC value and the average Cmax value, you know, the two primary determinates of rate and extent of absorption, were within the FDA's requirements, but the confidence limits exceeded the requirements.
Q. What do you mean by "exceeded"?
A. So I did see a study --
Q. Sorry, continue.
A. So I did see -- I did see a study

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that failed the FDA's bioequivalence standards and the company did a root cause analysis -- I don't remember which one it was right now -- and found that it was a -- a change in the size of the microparticles when they did the tableting, and so they went back and reformulated the tablet and redid a bioequivalence study -- and its one of the ones that's in here -- that then met the FDA standards after the reformulation.
Q. You don't recall what company that is?
A. I don't. I'd have to go back and look through all those files again.
Q. Do you know what -- if they're API?
A. Again, I -- I don't know off the top of my head whether they made their own or whether they purchased it.
Q. You don't know if they were getting their API from ZHP?
A. I don't, off the top of my head.
Q. And do you happen to know if wherever they were getting their API from sent them the same API later on that they passed their bioequivalency study with?

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A. I seem to recall that they were using the same API. It was more the tableting process that needed to be revised.
Q. Was it the size of the granules of the valsartan API that was causing the bioequivalency studies to fail?
A. No. It was the size of the particles that are used as part of the tableting process. So, yes, valsartan was in that particle, and I don't know whether there was NDMA in there or not. But based on the internal report for that company, it had nothing to do with the API; it was the tableting process.
Q. What are you basing that on, the -- it's the tableting process and not the API?
A. Their own internal root cause analysis.
Q. But you can't point me to which Defendant you're discussing or the document that you're relying on?
A. I could. It might take me two or three hours to sift through the files.
Q. That's okay. I think we'll probably get to it later.
MR. VAUGHN: Let's go to page 36,

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Melisha, and start on line 586.
BY MR. VAUGHN:
Q. All right. We're talking about Torrent's ANDA 202377. And so this would, again, be the valsartan plus amlodipine, correct?
A. Yes.
Q. And the bioequivalency studies within this ANDA is PK-09-192, PK-09-193 and PK-10-023, and you note that these were conducted between May and July of 2010, correct?
A. Yes.
Q. Is it your opinion that Torrent's valsartan was contaminated with nitrosamines in May of 2010?
A. Again, it may have been. I -- I do not know.
Q. And so, again, if Torrent's valsartan was not contaminated with nitrosamines in 2010, then these studies don't actually tell you anything specifically on if nitrosamines impact the bioequivalency of valsartan plus amlodipine, correct?
A. Again, not in and of itself, but -- but if it did contain it, then it does tell you that.

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Q. But you have no idea if Torrent's valsartan was contaminated back in 2010 with nitrosamines, do you?
MR. FOWLER: Asked and answered.
THE WITNESS: I -- I do not know.
BY MR. VAUGHN:
Q. Do you know what the purpose was of them doing two fasting studies at different milligrams?
A. I -- I don't. I don't recall seeing why that selection was made. Again, I know they're required by the FDA to do the highest dose. I don't know why they chose the 160 in addition, so I -- I really don't know. I certainly don't recall seeing in the documents I had access to, that it was explained.
Q. Is there any reason why on the fed study the bioequivalency range is on the low end and on the fasting studies it's on the high end?
MR. FOWLER: Objection to form.
THE WITNESS: I do believe that it's been reported that there's a small reduction in systemic exposure to valsartan when taken with food compared

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to not being taken with food. But then it's in the package label that the -- that small reduction is of -- not of any clinical significance. And so patients in the package labels are instructed that they can take it with or without food and it won't alter the ultimate response to the drug.
BY MR. VAUGHN:
Q. That small reduction in systemic exposure to valsartan when taken with food, that should be the same for the brand name and the generic, correct?
A. Yes.
Q. Then why is the generic low on the fed studies but high on the fasting studies?
MR. FOWLER: Objection, form.
THE WITNESS: I don't think it's only because of whether it's fed or not fed. I think tablet performance, if you go back and look through some of these, some manufacturers, even in a fasting state, their AUCs are a little higher than Diovan and some are a little lower than Diovan. So it -- it's not purely

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only capable of being different because of a function of being fed or not.
BY MR. VAUGHN:
Q. Do you -- in relation to valsartan, do you have an opinion if fasting or fed bioequivalency studies are harder to pass?
A. I have no opinion that they're any harder to pass.
MR. VAUGHN: All right. Page 37.
BY MR. VAUGHN:
Q. All right. In the Comparison part now is Diovan HCT. Is HCT the same as HCTZ?
A. Yes. Novartis, in their branded name, they don't use all four letters. They just use three of them. Whereas in the generic pharmacology vernacular, we always use the four letters of HCTZ.
Q. Okay. And so this section is now on the combination of valsartan plus HCTZ pills, correct?
A. Correct.
Q. And this is Aurobindo ANDA 202519 that you're discussing in this paragraph, correct?
A. Yes.
Q. And the studies within that ANDA

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are 304-09 and 305-09. And you note that those were conducted -- well, actually, you don't know what year those were conducted, do you?
A. Yeah, I don't know why I didn't put that in there. I tried to be consistent in -- in including the actual dates. And so I don't know if I received only a summary report that didn't have them.
What I could do, though, is go to the FDA's website and put in the ANDA number, and you can get from the website the date that the FDA approved the ANDA. So I did have that.
Q. Based on Aurobindo's naming structure of their studies, does that -09 indicate anything to you?
A. I can't say that I paid attention to whether that was a 09, like 2009 study or not, so I don't know for sure. It may have been the ninth production product or -- you know, I have no idea.
Q. Or a 2009 manufacturing date of the product?
A. Could have been.
Q. Well, let's just assume, then, that this was done in 2010. If this was done in

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2010, do you have an opinion as to if Aurobindo's valsartan was contaminated with nitrosamines?
A. I don't know. It may have.
Q. And if the ANDA wasn't approved until March of 2013, the studies were definitely done in advance of that, correct?
A. They were definitely done in advance of 2013, yes. For sure.
Q. And the manufacturing date of the valsartan would have been even earlier than the bioequivalency studies, correct?
A. By some, usually, a few months time frame.
Q. And so you're unaware if the product tested in these bioequivalency studies was contaminated with nitrosamines, correct?
MR. FOWLER: Asked and answered.
THE WITNESS: Correct, I'm unaware of that. They may have been.
BY MR. VAUGHN:
Q. And if Aurobindo's valsartan was not contaminated with nitrosamines at the time that these studies were being conducted, these bioequivalency studies don't actually tell you anything on if nitrosamines impact the

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bioequivalency of the valsartan plus HCTZ, correct?
A. And, again -- and the same if they do.
But without an overlapping mechanism, it doesn't matter whether it's in there or not.
Q. And so none of these studies that we've looked at actually matter to you, do they, because you don't know if any of them have nitrosamines in the drug product?
MR. FOWLER: Objection to form.
THE WITNESS: No, that's not what I said about them not mattering. I'm saying whether NDMA was in there or not doesn't matter because the bioequivalence would be retained.
BY MR. VAUGHN:
Q. So in your expert opinion, it doesn't matter if the study is using a drug product with nitrosamines in order to figure out if nitrosamines impact the bioequivalency of the drug?
A. It is my expert opinion that whether they were in there or not would not affect

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the bioequivalence. And -- and if I recall from having read one of Plaintiff expert's depositions, Dr. Najafi, I believe, I think he said the same thing. It didn't matter whether it was in there or not; it wouldn't have affected the bioequivalence.
Q. If there are bioequivalency studies that were conducted on valsartan that was known to be contaminated, would you want to review those studies?
A. Of course if I had them, I would review them.
Q. Would you give more weight to the studies that had no nitrosamines impurities in them versus ones that did have nitrosamines impurities in them?
A. No, because they're not going to show any difference, so it wouldn't have any difference to me at all. Wouldn't change my conclusion, it would only support my conclusion.
Q. And so without looking at the studies, you can already determine that they're not going to show any difference?
A. To the best of our scientific capability through mechanisms whereby there would

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be an effect on bioequivalence, and those mechanisms do not exist.
MR. VAUGHN: All right. Go on to page 38.
BY MR. VAUGHN:
Q. All right. And you're now discussing at line 613 Princeton ANDA 206083. And again, this is for valsartan plus HCTZ, correct, Doctor?
A. Yes.
Q. And within the ANDA you note bioequivalency studies H052-12 and H053-12, and you note that these were both done in 2012, correct?
A. Yes.
Q. And do you have any opinion on if Princeton's valsartan plus HCTZ was contaminat- -- contaminated with nitrosamines in 2012?
A. I don't personally know that. They may have been.
Q. And if Princeton's valsartan was not contaminated with nitrosamines in 2012, these studies don't actually tell you if nitrosamines are going to impact the bioequivalency of

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Princeton's valsartan plus HCTZ, correct?
A. Correct, in that -- in and of itself. But, again, with the presence of milligram quantities compared to NDMA microgram quantities, without overlapping mechanisms, it adds to the body of -- of my knowledge that there's no reason to expect that NDMA would have any effect on bioequivalence at all.
Q. Okay. And in the paragraph starting at line 622, you are discussing ANDA 091654, which is for Torrent's valsartan plus HCTZ, correct?
A. Yes.
Q. And then you note Studies PK-09-23 and PK-09-024, and you note that these bioequivalency studies were conducted in March of 2009, correct?
A. Yes.
Q. And do you have any opinion if Torrent's generic valsartan plus HCTZ was contaminated with nitrosamines back in 2009?
A. I do not know. It may have been.
Q. And if Torrent's valsartan plus HCTZ was not contaminated with nitrosamines back in 2009, then these bioequivalency studies don't

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actually tell you anything on if nitrosamines impact the bioequivalency of valsartan plus HCTZ, correct?
A. Correct, to a certain degree. But, again, without the overlapping mechanisms and the fact that it may have had it in there, then I -- I don't think this is changing my conclusion at all.
MR. VAUGHN: Page 39.
BY MR. VAUGHN:
Q. All right. Paragraph starting line 626, you note Mylan data on bioequivalency studies comparing generic valsartan/HCTZ to Diovan/HCT, but you don't reference an ANDA on this one.
Is there a reason for that?
A. It was either not identified in the files that I received or that I could not find it directly at the FDA website to put a specific ANDA number in.
Q. What do you mean by "not identified in the files" you received?
A. As I said before, some of these files I received were very lengthy and very comprehensive, and some of them I received were:

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Here's our bioequivalence result for Diovan/HCT versus our equivalent product.
And so it -- I may have in some cases had a much more limited amount of information that came with the file that had the BE data in it.
Q. And so for some of the files, you were not able to review all the data, correct?
A. I was able to review the relevant bioequivalence data, yes.
Q. And the Mylan studies, that you were discussing in this paragraph, you note were conducted in May of 2005, correct?
A. Yes, I did have that information.
Q. And did you have any information on if Mylan's valsartan plus HCTZ was contaminated with nitrosamines back in 2005?
A. I have no knowledge of that. It may have been.
Q. Your opinion today is that Mylan's valsartan might have been contaminated going all the way back to 2005?
A. Do not know.
Q. And if Mylan's valsartan plus HCTZ was not contaminated back in 2005, then these

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bioequivalency studies don't actually tell you anything on if nitrosamines impact the bioequivalency of valsartan plus HCTZ, correct?
A. They indirectly do, as I -- as I've stated before, because milligram quantities of HCTZ without an overlapping mechanism do not alter valsartan. So there would be no reason to expect that microgram quantities of NDMA or NDEA, without overlapping mechanisms, would have any effect on the bioequivalence.
So I -- I don't change my conclusion at all.
Q. Does that meet FDA guidance, that just if there's not a known overlapping mechanism, that you don't need to do bioequivalency studies?
MR. FOWLER: Objection: Form, foundation.
THE WITNESS: The FDA requires the bioequivalence studies irrespective of whether they do or do not have impurities in them.
BY MR. VAUGHN:
Q. If a drug has a different chemical in it, even if it's an excipient, does the FDA require additional bioequivalency studies?

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MR. FOWLER: Objection, form.
THE WITNESS: Make sure I'm understanding. Are you asking if two products have different excipients of the same active ingredient, would it require a bioequivalence study?
BY MR. VAUGHN:
Q. Yeah. If a generic drug that already passed bioequivalency studies added a new excipient, would the FDA require additional bioequivalency studies?
A. Probably not in humans. They, again, would probably be allowed to do a dissolution study that showed the same release characteristics.
Q. What are you basing that on?
A. Basing it on the FDA guidance for bioequivalence testing.
Q. Which FDA guidance on bioequivalence testing?
A. Probably the one that I referred to in my report.
Q. Do you know which year that one is?
A. I don't. I know they released a

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new one maybe last year, but I don't think there was substantial changes in it.
Q. Did you disagree with anything in the FDA's guidance?
MR. FOWLER: Objection, form.
THE WITNESS: I'd have to see what you're referring to.
BY MR. VAUGHN:
Q. As you're sitting here today, do you recall disagreeing with any of the FDA's guidance on bioequivalency studies?
A. As I sit here today, I do not recall that. But I don't know what you're referring to. It's -- I -- it's so vague, I can't -- I can't really answer your question.
Q. Are you giving any regulatory opinions in this litigation?
A. I'm giving no regulatory opinions in this case. I think there are other people that have been asked to provide opinions that are much more qualified than I on that.
Q. At the bottom of page 39, we are now in the section regarding valsartan plus amlodipine plus HCTZ, correct?
A. Yes.

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Q. And their reference drug is, again, Exforge HCT?
A. Yes. So this is a -- a three-drug combination now.
Q. Does Exforge HCT have amlodipine in it?
A. Yes.
Q. And is Exforge HCT what was also being compared to on the generic valsartan plus HCTZ but not amlodipine?
A. Valsartan plus amlodipine alone would be equivalent to the Exforge. Valsartan plus HCTZ would be equivalent to Diovan/HCT. And then valsartan plus amlodipine plus hydrochlorothiazide would be equivalent to the Exforge HCT.
Q. Understood. Thank you for that clarification.
And so that last paragraph on page 39, you are discussing Teva's ANDA 2004354, valsartan plus amlodipine plus HCTZ, correct?
A. Yes.
Q. And I don't see that you identified the studies in this ANDA. Do you see if you did, Doctor?

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A. I don't see a specific study number.
Q. Is there a reason for that?
A. It -- it wouldn't have been an oversight on my part, so it must not have been that the actual study number was provided in the materials I was given to review or that I asked for to review.
Q. And if the Defendants had that information, you would have expected that they would have given it to you, correct?
A. Yes. I'm sure they had it, and it wasn't in the materials that I received.
Q. You were sure that the Defense attorneys had it, but they did not give it to you?
MR. FOWLER: Objection, form. He didn't say that.
THE WITNESS: Yeah, what -- what I meant to -- to mean is that the file that came through Defense lawyers to me from Teva, Teva must not have provided it in what was sent to them to give to me. So I had no direct contact with Teva.
BY MR. VAUGHN:

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Q. And these studies done in Teva's ANDA 200435, they were conducted in 2009, correct?
A. Yes, I did have that information.
Q. And do you have an opinion on if Teva's valsartan was contaminated with nitrosamines back in 2009?
A. I don't know if it was or not.
Q. And therefore, if it was not contaminated with nitrosamines back in 2009, these studies don't tell us anything on if nitrosamines impact the bioequivalency of Teva's valsartan plus amlodipine plus HCTZ, correct?
A. Incorrect. Again, this is an -- an even more extreme example of making my point. You now have three drugs in milligram quantities that don't have overlapping mechanisms of metabolism that show no altered bioequivalence.
Q. And it's your opinion that that supports that nitrosamines can't alter the bioequivalency of these drugs?
A. The absence of an overlapping mechanism of metabolism or distribution, absolutely, I believe that.
Q. Did you discuss any other bioequivalency studies in your expert report,

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other than the ones that we have covered?
A. I'm assuming you went through every one that -- I haven't going back to -- to do a head count, but I'm assuming it's every one. So I have no additional ones that I had access to.
Q. And all of the ones that we reviewed, none of them were you aware if nitrosamines were in the drug product, correct?
MR. FOWLER: Asked and answered.
THE WITNESS: I don't believe that I -- I don't know, but I'm under the impression that some of them did.
BY MR. VAUGHN:
Q. Which ones are you under the impression had nitrosamines in them when they were conducting the bioequivalency studies?
MR. FOWLER: Objection, asked and answered.
THE WITNESS: I -- I don't know which ones, but I'm under the impression that some did.
BY MR. VAUGHN:
Q. Do the --
A. I'm even under the impression -- I'm sorry.

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I'm even under the impression that some of the Diovan may have had nitrosamines in them as well. Again, I don't think it alters my conclusion at all because it would have no impact on the bioequivalence studies.
Q. Did the Defense attorneys tell you to assume that some of the generic valsartan that was studied in these bioequivalency studies were contaminated with nitrosamines?
A. Defense attorneys did not tell me to assume anything. They have access to information through other depositions and things that I'm not aware of, but they did tell me that there was the likelihood that some of these generics contained NDMA even before ZHP identified that it had NDMA.
Q. How far back did the Defense attorneys tell you that the contamination likely goes?
A. I was not given a time frame. I do not know that.
Q. And so when you testify --
A. I think it was --
Q. Sorry, go ahead.
A. Yeah. I think I was going to say

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that, again, in -- in reading Dr. Najafi's deposition, I think he was the one that concluded or -- or stated that even Diovan had some NDMA in it. And so I'm saying it doesn't matter. The bioequivalence, and therefore the systemic exposure, and therefore the systemic effect of generic valsartan products are completely independent of whether there is or isn't NDMA in there or whether it was in the branded products or not.
Q. Earlier you testified that you were under the impression they had nitrosamines in them when they were [sic] conducted the bioequivalency studies. How are you under that impression?
MR. FOWLER: Objection: Form, vague.
THE WITNESS: Again, I'm -- I'm under the impression from discussions I've had with counsel that there were some generic manufacturers that have identified that they might have had NDMA even at the time that some of these bioequivalence studies were conducted.
BY MR. VAUGHN:

Q. Did you refute --
A. And it --
Q. Sorry.
A. -- doesn't matter. No. I was just going to say it doesn't matter, because it's not going to have any effect on the bioequivalence anyway.
Q. Did you review any documents that indicated that any of the drug products tested in these bioequivalency studies were actually contaminated with nitrosamines?
A. I have -- I have seen no such documents, no.
MR. VAUGHN: Why don't we go off the record.
THE VIDEOGRAPHER: The time is now 11:53 a.m. We are off the record.
(Lunch recess observed.)
THE VIDEOGRAPHER: The time is 12:38 p.m. We're back on the record.
BY MR. VAUGHN:
Q. Welcome back, Dr. Bottorff.
MR. VAUGHN: Melisha, can we pull up the 2011 FDA Guidance for Submission of Summary Bioequivalence Data for

ANDAs?
And this will be Exhibit 4.
(Exhibit 4 was marked.)
BY MR. VAUGHN:
Q. All right. Have you reviewed this document previously, Dr. Bottorff?
A. Yes, I have.
MR. VAUGHN: Melisha, can we go to PDF page 4? It's page 1 at the bottom of the document.
BY MR. VAUGHN:
Q. All right. I'm looking at line 19. Actually, it starts on line 18. Do you see, Doctor, where it says: "FDA's final rule on requirements for submission of bioequivalence data requires an ANDA applicant to submit data from all bioequivalence studies the applicant conducts on a drug product formulation submitted for approval, including studies that do not demonstrate that the generic product meets the current bioequivalence stamp criteria"?
A. I see that.
Q. And at the top of this document, it does say that the document contains nonbinding recommendations, but the sentence I just read has

a citation down to the Final Rule: "Requirements for submission of bioequivalence data that was published in the Federal Register on January 16th, 2009," correct?
A. Correct.
Q. And do you agree that an ANDA applicant should submit all of their bioequivalency studies, even studies which failed?
MR. FOWLER: Objection: Calling for a regulatory opinion, outside the scope.
THE WITNESS: I can sit here and read that the same as you can, but, again, I -- I don't have opinions on -- on regulatory issues.
BY MR. VAUGHN:
Q. And so you also don't have an opinion on if they're supposed to submit failed bioequivalency studies that happened after the submission of their ANDA?
MR. FOWLER: Same objection.
THE WITNESS: Yeah. Again, I have no opinion on that.
MR. VAUGHN: All right. Melisha, let's go to the -- the FDA's 2021 Draft

Guidance now.
And this will be Exhibit 5.
(Exhibit 5 was marked.)
BY MR. VAUGHN:
Q. Doctor, is this the 2021 Guidance that you were referencing earlier in this deposition?
A. Yes. It's the one that I said I'd also seen. It existed in a -- in a draft format.
MR. VAUGHN: Go to PDF page 8, Melisha. It's going to be page 5 at the bottom. And it might be PDF page 9.
MR. FOWLER: So let me just have a running objection to the relevance of this 2021 Guidance to this case, so I don't interrupt you.
BY MR. VAUGHN:
Q. All right. Doctor, on line 147 where it says: "If a drug product is intended for use in both sexes, the applicant should include similar proportions of males and females in the study or provide a justification supporting the use of a single-sex population."
Why is that?

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MR. FOWLER: Objection, calls for a regulatory opinion.
Go ahead, to the extent you can answer.
THE WITNESS: Yeah, I -- I don't know why, but I know it's done. On my CV, I don't know if it was noted or not, but I've been added to a National Investigational Review Board for a company called Advarra. And we review Phase 1 protocols on a weekly basis from a variety of pharmaceutical companies, and I can tell you that the vast majority of them have about an equal number of males and females.
Provided, there's all kinds of stipulations about making sure that it's females either of nonchild-bearing potential or who have some of the -- the highest level of -- of pregnancy prevention techniques in place.
BY MR. VAUGHN:
Q. And designing a bioequivalency study like this with -- using both sexes, is that something that's new as of 2021, or does that date

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back before 2021?
A. I, again, can't tell you when that started, but I know it's being practiced as of today. Since I've been on that IRB, I've seen numerous trials come through that are practicing this standard.
Q. And you testified that you've done bioequivalency studies dating all the way back to college, correct?
A. Yes.
Q. And in those bioequivalency studies, was there a fairly equal number of males and females in the studies?
A. There were not. And that was, like, 1982-1983. So it was a fair number of years ago.
Q. And do you have any idea when that started to change, that they were recommending to use equal numbers of male and females in the study?
MR. FOWLER: Asked and answered.
THE WITNESS: I -- I do not.
BY MR. VAUGHN:
Q. And you do not know why that's recommended?

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A. I'm not sure. I -- I really don't know. Maybe to broaden the populations of people that get exposed to the early phases of drug development.
Q. In a drug like valsartan, it is given to both males and females, correct?
A. Well, if the females aren't pregnant. There's a Black Box Warning: Do not give it to pregnant females.
Q. And so is that one reason that you'd want to have both sexes in your studies, is so you understand how it works in both males and females?
MR. FOWLER: Form.
THE WITNESS: Again, I don't know what led to a change, and I don't know when the change occurred.
BY MR. VAUGHN:
Q. Line 153, it notes: "If a drug product is prom- -- predominantly intended for the use in the elderly, the applicant should include as many subjects as possible at or above age 60."
Do you know why that's recommended?
A. I'm assuming for what it actually

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says in that sentence, if it's predominantly intended to be used in the elderly.
Q. Do elderly metabolize drugs differently than young people?
A. Again, much like the previous question about cirrhosis, it's -- it's not a given. There are many, many studies that I've seen over the years of my career where the pharmacokinetics, and therefore the bioequivalence of a drug, were not altered just by being older. It's more likely the pharmacodynamics that change, sensitivity to the heart rate adjustments or -- it's more the pharmacodynamic end points that change with -- with aging, not so much the pharmacokinetic end point. Sometimes. Sometimes it does. It's not a blanket statement that -- that fits all.
Q. So it sometimes does.
Would that be a reason you'd want to actually test it in the population the drug is being given to?
A. Well, I mean, that's one reason.
Q. Can you give me additional reasons?
A. Well, maybe, like I said, because

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they're sensitive, and so you might want to do studies with lower doses, if you didn't do bioequivalence studies with lower doses before.
Q. In your opinion, what's the average age of a valsartan user?
MR. FOWLER: Objection: Form speculation.
THE WITNESS: I -- I could not even come close to what the right answer would be, but I can tell you when you look at the FDA-approved indications for hypertension, heart failure and postmyocardial infarction, those are not going to be 18-year-olds, 20-year-olds, 25-year-olds. They're going to be 50-, 60-, 70-year-olds.
BY MR. VAUGHN:
Q. And then looking at line 169, it reads: "In such situations, applicant should attempt to enroll patients for whom the drug is intended to treat and whose disease process and treatments are stable for the duration of the study."
Do you see that, Doctor?
A. Yes.

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Q. Do you agree with that statement?
A. Well, not in isolation without the sentence before it. Because in some situations, the drug has a safety consideration that would preclude its use in healthy subjects. So I'm thinking -- what jumps out at me at that point are new cancer drugs.
Q. Would --
A. You would only want to test those in patients with stable cancer.
Q. Thank you for that clarification.
Now, when it applies to valsartan, would there be any reason why it should not be tested in the patient population it's intended to treat?
MR. FOWLER: Objection: Form, mischaracterizing.
THE WITNESS: And I -- I don't think -- again, I think this starts getting into a realm of -- of regulatory, but I don't think the companies who did bioequivalence testing in younger, healthy, normal volunteers was anything other than what the FDA expected to see.

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BY MR. VAUGHN:
Q. And you see the next line, it says: "Investigational New Drug Application may be required for certain products (such as cytotoxic products.)" And then it cites to 21 CFR 312.2(c).
Do you see that, Doctor?
A. Yes.
Q. Were you aware of that?
A. Well, I've previously read this, but -- so, yes, I was aware of it.
Q. What is an Investigational New Drug Application?
A. That's for a drug that's never been given to humans, and so you're looking to get approval to start testing in humans.
Q. Is valsartan cytotoxic?
A. No.
Q. Is NDMA cytotoxic?
MR. FOWLER: Form.
THE WITNESS: I -- I don't believe so, in what the definition of cytotoxic is, to my recollection. I think of cytotoxic as either antibiotics that are cytotoxic to an organism or

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cancer drugs that are cytotoxic to cancer cells.
BY MR. VAUGHN:
Q. What is your definition of cytotoxicity?
A. It's a drug that kills cells. And we're talking here about active ingredient, so it's an active ingredient whose intent for use is cytotoxicity.
MR. VAUGHN: All right. If we can go to page 22 at the bottom, Melisha. I'm not sure what PDF page it is.
BY MR. VAUGHN:
Q. All right. I'm looking at the line 846, Handling of Outliers. Doctor, you see this first sentence says: "Applicant should not remove data from the statistical analysis of bioequivalency studies solely because that data are identified as statistical outliers."
Do you agree with that statement?
A. Well, yes, it's in the FDA document.
Q. And you agree that a manufacturer shouldn't remove statistical outliers even before

2021, right?
A. Again, the way in which the data are handled can vary. Some of this is relating to the fact that some patients or subjects will later to [sic] be found to have some reason for it, and some of that could be biologic. I mean, I don't know the details behind it. Starts getting into a statistical handling of the data.
That's not really what I -- what I've done.
Q. You have not done a statistical handling of the data of any of these bioequivalency studies?
A. The kind that are down below in 870, I have, but not removal of outliers, I've not.
Q. Did you notice in any of the bioequivalency studies that you reviewed that the manufacturer removed outliers?
A. Never saw any reference to that at all.
Q. Then going to line 854, it notes that: "Data from redosing studies are not considered as evidence to support removal of outlier data from the statistical analysis. Note

that all subject data should be submitted and potential outliers flagged with appropriate documentation as part of the submission."
And you agree with that as well, correct, Doctor?
A. Yes, it's -- it's in their document.
MR. VAUGHN: Let's pull up the depo notice, Melisha.
It's going to be Exhibit 6.
(Exhibit 6 was marked.)
BY MR. VAUGHN:
Q. Have you seen this document before, Dr. Bottorff?
A. Yes, I have seen it.
Q. When was this document given to you?
A. I believe it was forwarded the day -- well, I don't know in relation to when it was received by -- by GT, but I received it in an e-mail probably earlier this week.
Q. And did you help GT in responding to this document request?
A. We went through it line-by-line or -- or paragraph-by-paragraph, and I was asked

what I had in relation to these document requests, and I either provided answers or what was requested.
Q. Approximately how many documents did you send to GT in relation to this document request?
MR. FOWLER: Objection: Form, vague, time frame.
THE WITNESS: Well, I mean, if you want to go through one-by-one.... But in No. 1, I did not send invoices because they had them already.
BY MR. VAUGHN:
Q. Oh, Doctor, I just mean in total, if that helps you. Just cuts the time up.
MR. VAUGHN: What's your objection?
MR. FOWLER: You said -- you mean in total. You mean a total of documents in re- -- sent in response to all 15 requests? I don't understand --
MR. VAUGHN: Yeah, that's exactly what I'm asking. Yeah. Out of all the documents requested --
MR. FOWLER: As opposed to

counting?
MR. VAUGHN: -- in this document, I asked him approximately, how many he sent to GT.
THE WITNESS: I'm running down to see. I have my recollection in my head, but I wanted to look at each of the points to make sure that I didn't miss something. But the only thing that I had that I could give were the notes that I was under the impression were sent to you.
I had no PowerPoints. I had no tables and charts. I had no books. Any of the other things that were requested here, I didn't have any- -- anything to provide.
BY MR. VAUGHN:
Q. Your notes were produced to us. I do appreciate you getting those to the Defense attorneys. And it was both the notes for the general causation expert report you did and the class action expert report you did.
Had you previously given GT's Defense attorneys your notes for the general

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causation expert report?
A. Yes, I had.
Q. And when was that?
A. I'm assuming in response to the exact same kind of document prior to the deposition for -- for the general causation.
MR. FOWLER: They were provided to you at the time of the general causation deposition, Mr. Vaughn.
MR. VAUGHN: Did I say they weren't?
MR. FOWLER: Your question suggested otherwise, but I just want to be clear on this record.
BY MR. VAUGHN:
Q. Doctor, are you aware that the Defense produced 16,632 documents 48 hours ago for your reliance materials?
A. No. The -- when you combine my reliance materials from the first phase of litigation to this phase, there's a lot of -- a lot of articles that have been looked at and read and a lot of multipage documents, like the Guidance for Industry that we looked at a while ago. So did I do a head count of those? No, I

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[redacted]

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BY MR. VAUGHN:
Q. And 16,632 sounds kind of unbelievable, doesn't it?
MR. FOWLER: Form.
THE WITNESS: Not to me, if that's what's on there. I didn't count them.
BY MR. VAUGHN:
Q. And so you believe that you've identified or sent 16,000 documents to the Defense attorneys?
MR. FOWLER: Mischaracterizing.
THE WITNESS: Again, what got sent to you, I have a copy of. I haven't counted the files. I mean, I don't -- I don't know.
MR. VAUGHN: Melisha, let's pull
[redacted]

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[redacted]

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[redacted]

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[redacted]

Page 116

[redacted]

BY MR. VAUGHN:

Q. Well, setting this document aside, do you agree that an ANDA that includes unreliable data developed at a tainted facility is not and never was substantially complete?

MR. FOWLER: Objection. You're calling for a regulatory opinion. You've already asked the doctor if he has those.

THE WITNESS: Yeah, that looks like a regulatory thing that I'm not offering opinions on. I don't know what

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constitutes, in the FDA's mind, a tainted facility and -- and what level of taint they're talking about and what should happen as a result of that. I -- I'm -- I'm not offering any opinions on those.

MR. VAUGHN: All right, Melisha let's go to page 3. Two pages later.

BY MR. VAUGHN:

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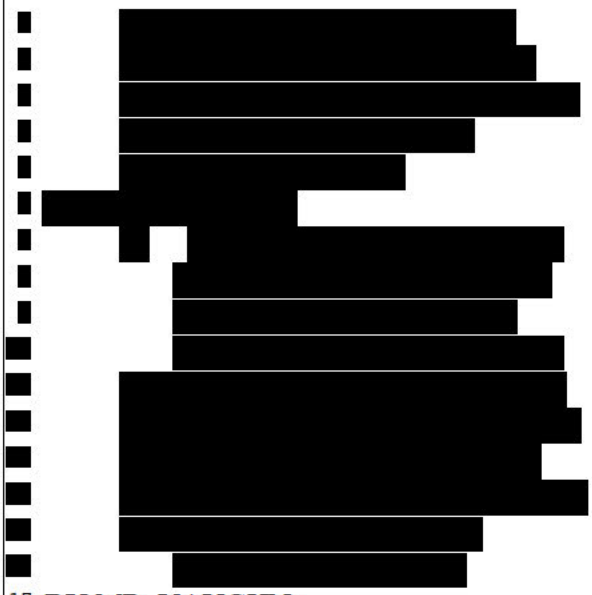

BY MR. VAUGHN:
Q. So, Doctor, if a bioequivalency study is -- if the manufacturer is deleting the failed test results and retesting the samples until it achieves the results it sought, would you consider those bioequivalence studies to be legitimate?
MR. FOWLER: Objection, form.
THE WITNESS: Again, this

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is -- this is all regulatory. I have no opinion on the regulatory.
BY MR. VAUGHN:
Q. Did you not evaluate the legitimacy of the bioequivalency studies that you opined on?
A. Yes, and they had approved ANDAs. So they're in a different ball park than what this is.
Q. Did you evaluate the underlying studies of the bioequivalency studies to see if any -- scratch that.
Did you evaluate the underlying data of the bioequivalency studies to see if failed testing was deleted and retested until it got an accurate result and then submitted the accurate results to the FDA?
A. Again, as I testified this morning, I only saw one instance of what was a failed test result, and it was included. My only exposure to that was what I testified to this morning.
Q. So you've seen one failed test result. Have you seen any indication of companies retesting samples until they get a different

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result?
A. Other than what you just handed me, no.
Q. And if the companies in this litigation were doing that with their bioequivalency studies, would you consider those studies to be illegitimate?
MR. FOWLER: Objection: Form, outside the scope.
THE WITNESS: Again, that's a regulatory, and -- and I have no evidence that that occurred or didn't occur, either way.
BY MR. VAUGHN:
Q. Not from a regulatory side, from a just statistics side from when it comes to a bioequivalency study and the legitimacy of it. Do you consider a bioequivalency study legitimate if they retested the samples until they got the desired results?
MR. FOWLER: Objection: Form, scope, incomplete hypothetical.
THE WITNESS: Again, the one instance that I saw, there was a failed bioavailability study. They

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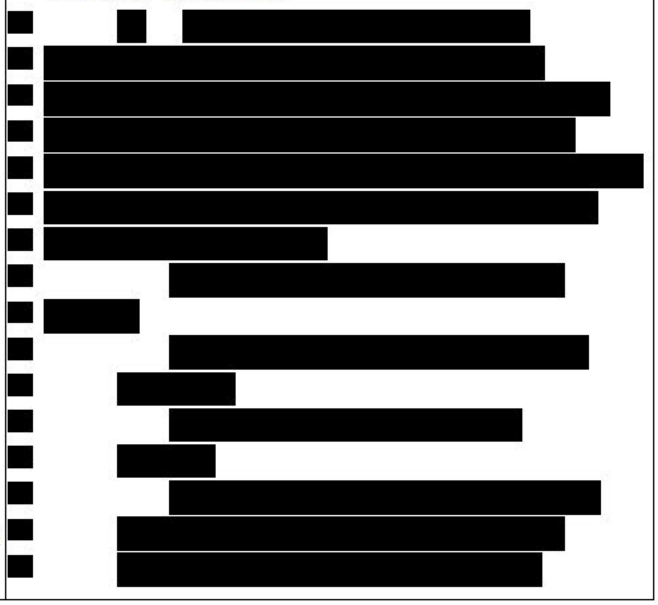
reformulated and passed, and I saw both examples. There was no attempt -- you know, no sixth time or ten-time attempt or multiple attempts. It was a one-time reformulation, and it led to an approved ANDA.
MR. VAUGHN: Let's go to page 5, Melisha.
BY MR. VAUGHN:



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[redacted]
BY MR. VAUGHN:
Q. Did you look into where the bioequivalency studies were done for the various manufacturers?
A. Yes. Most of the time that -- that location was -- was provided in the summary reports, or in some cases in the individual patient, what they call Case Report forms, where -- all of their height and weight and lab values and, you know, side-effect monitoring. You know, all that was done on a form that was specific for the facility that conducted the bioequivalence study.
Q. Do you recall any of the facilities that conducted the bioequivalency studies?
A. Not specifically. I -- I can tell you that there were some that were in India, and I do recall that there was one in North Dakota.
Q. Do you recall if either of those companies or facilities had been cited for data

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integrity violations?
A. I have no idea.
Q. Did you not look into that in forming your opinions in this report?
A. I did not look into that. Again, these -- these were approved ANDAs. So whatever the FDA determined from the sites where those data were submitted, the FDA approved that.
Q. And the FDA can only base their decision off of what was provided to them in the ANDA, correct?
A. I'm assuming so.
Q. And if there are data integrity issues in the submission, how is the FDA supposed to identify that?
MR. FOWLER: Objection: Form, incomplete hypothetical.
THE WITNESS: Again, I think it starts spilling into regulatory, what the FDA uses as information to decide what they will do next. But I think if they invalidated an ANDA, they would pull the drug.
BY MR. VAUGHN:
Q. And so if there's shown that

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there are data integrity issues with the studies submitted in the company's ANDA and the FDA becomes aware of it, they can pull the ANDA, correct?
MR. FOWLER: Objection: Form, scope, regulatory opinion.
THE WITNESS: Again, I -- I think it's a regulatory opinion, so I can only conjecture. But that would -- that would be what would make sense to me.
[redacted]

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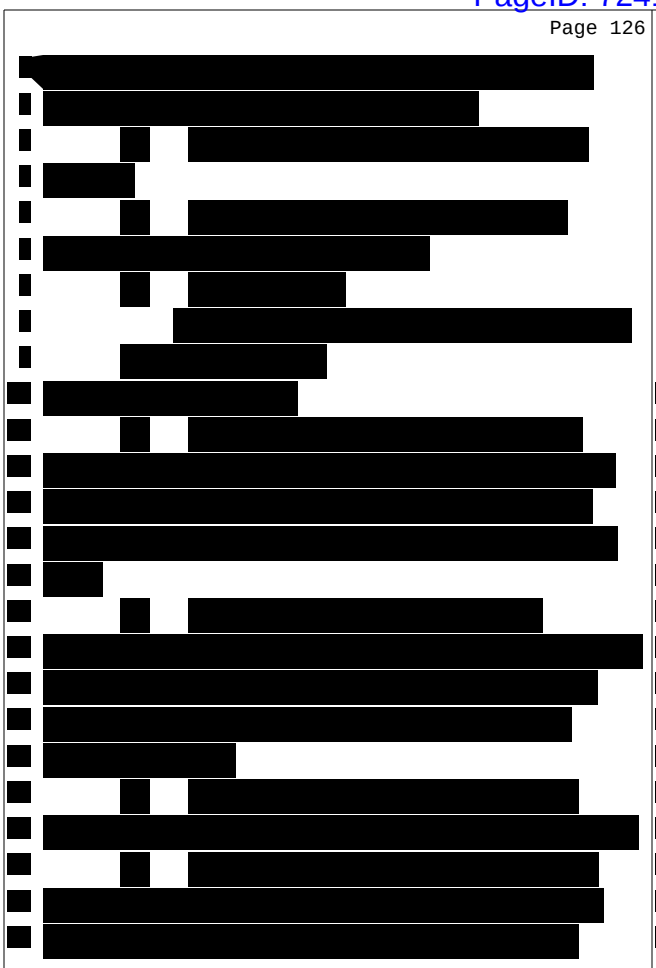

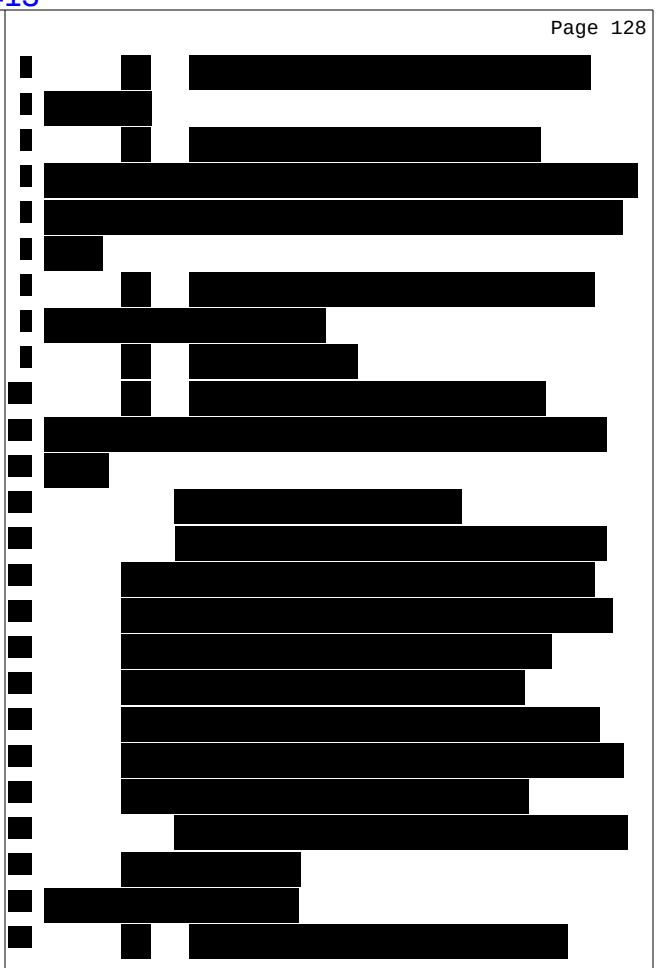

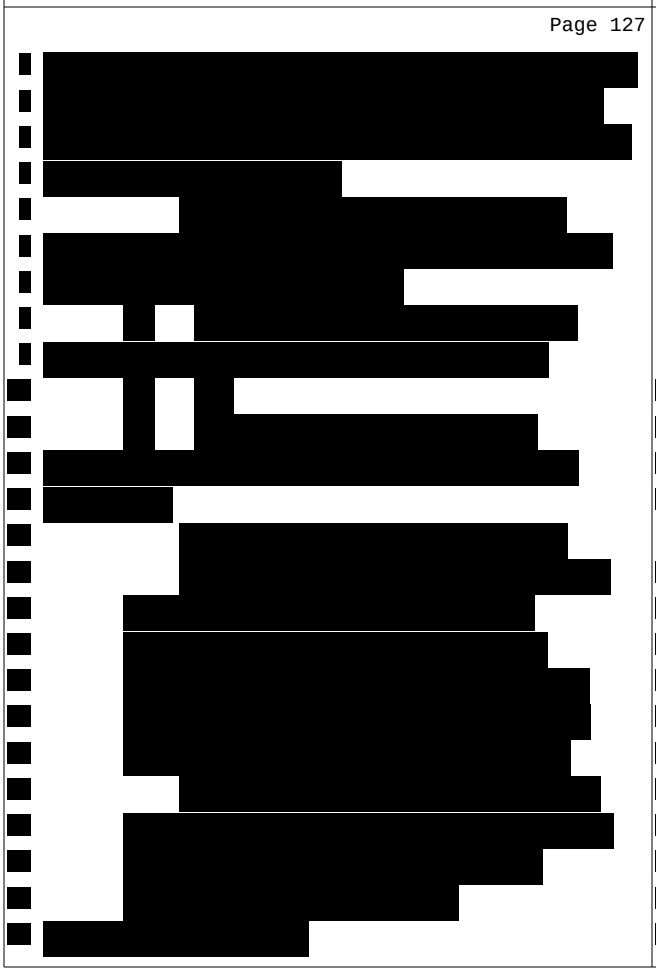

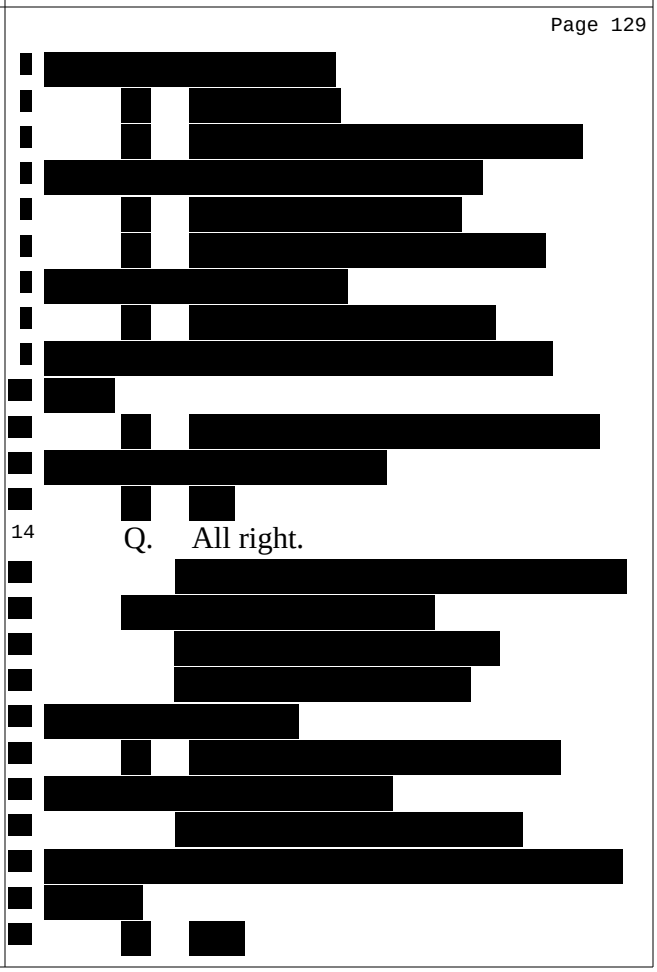

14 Q. All right.

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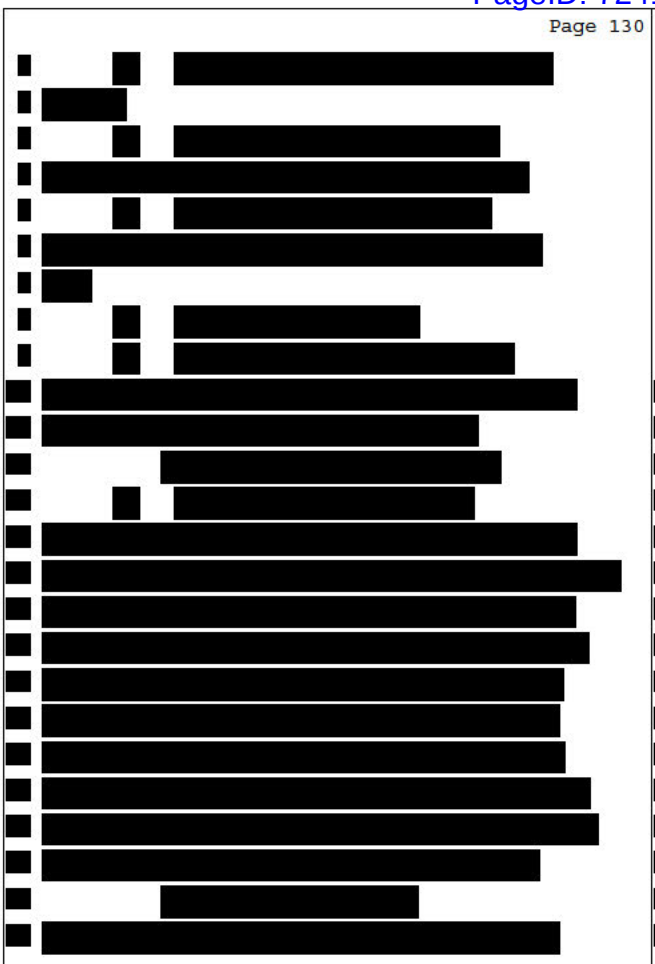

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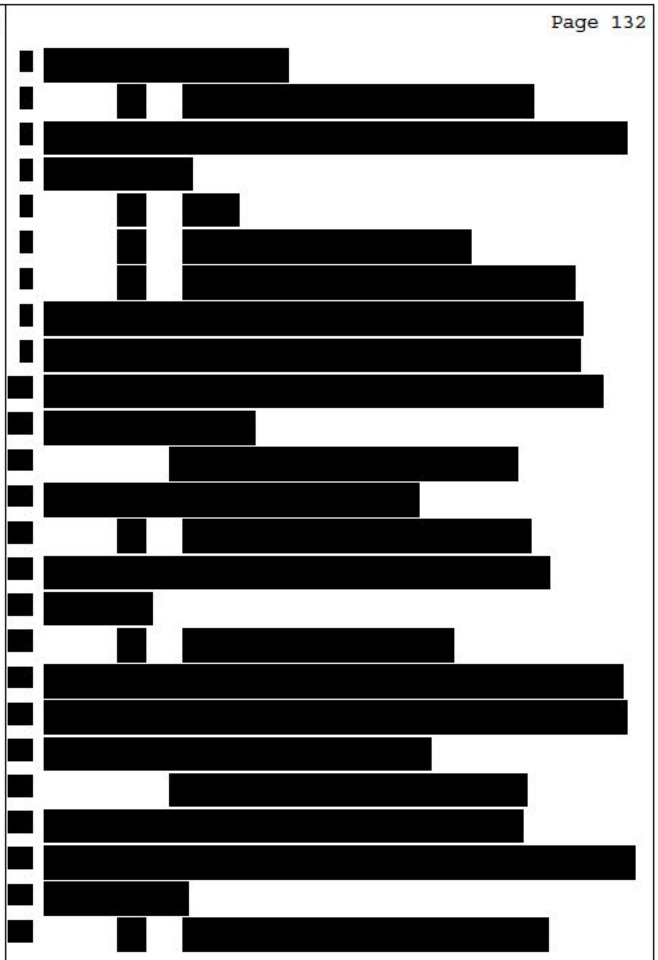

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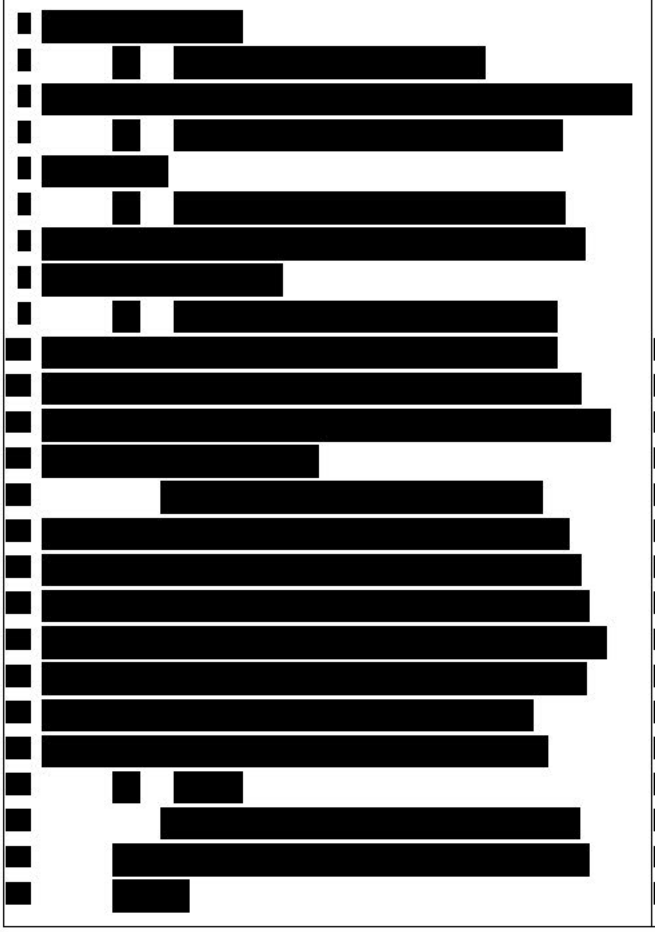

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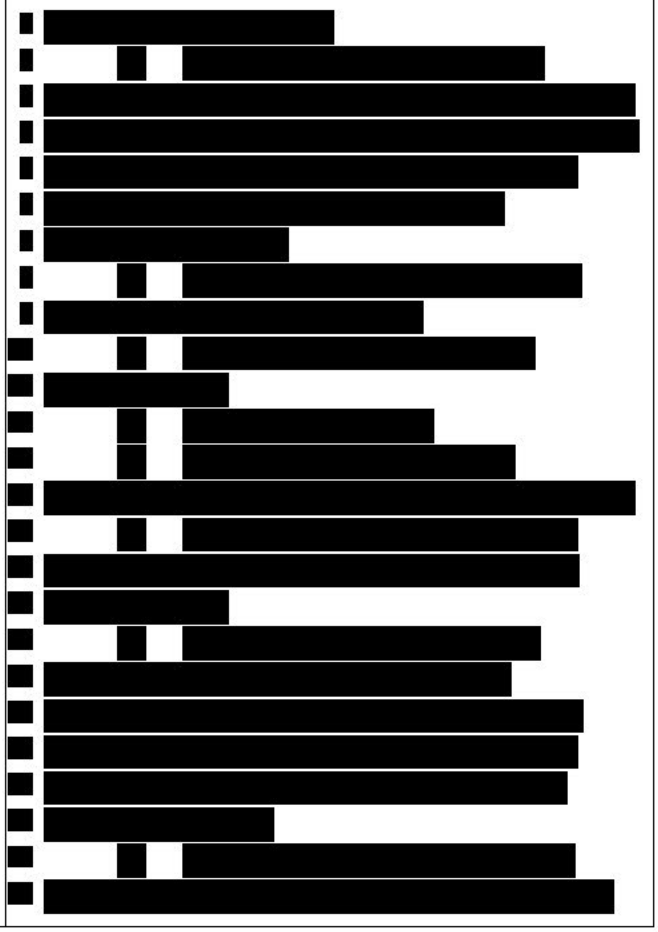

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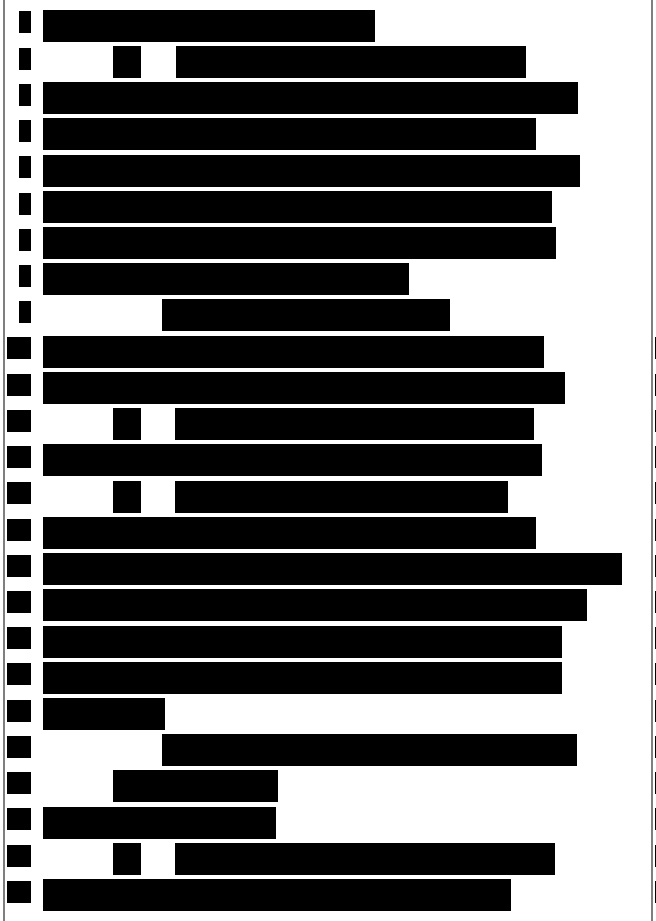

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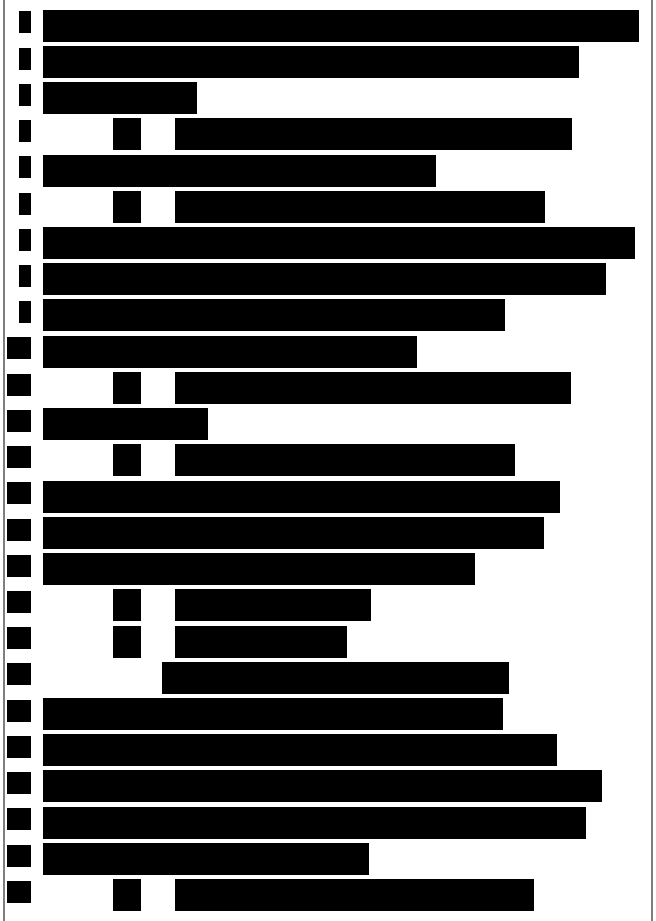

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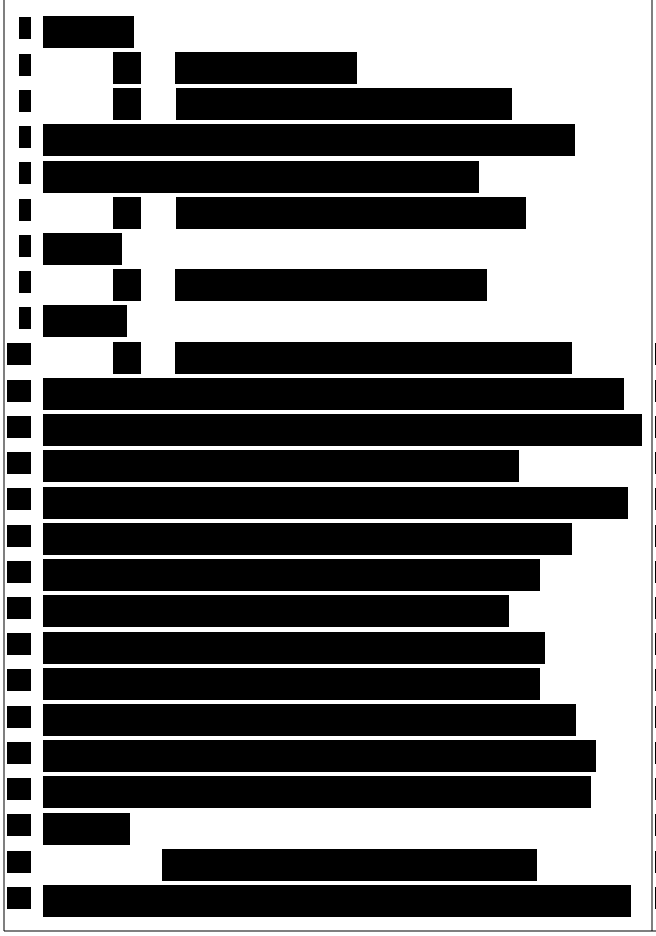

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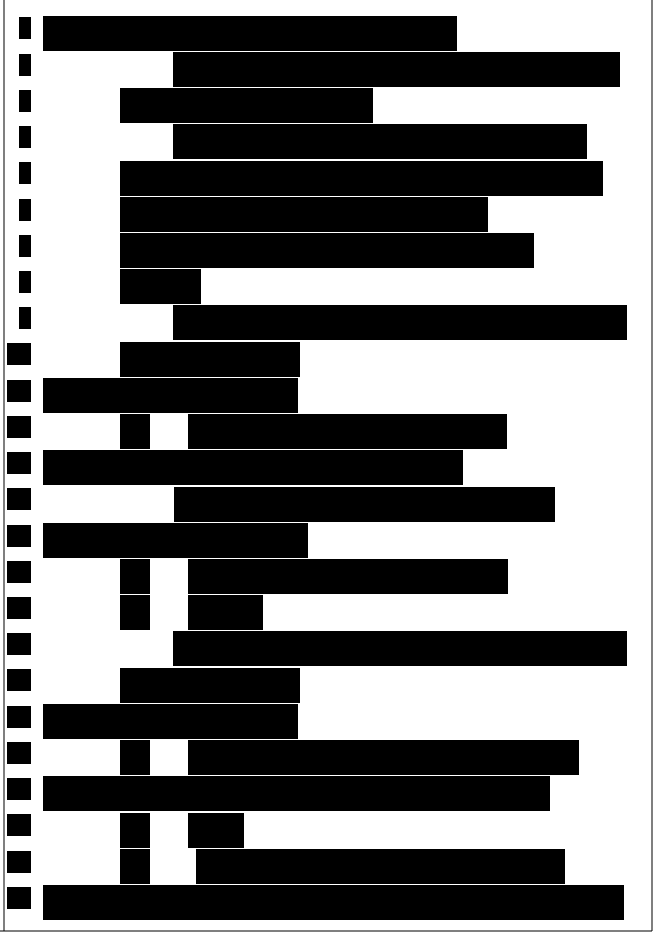

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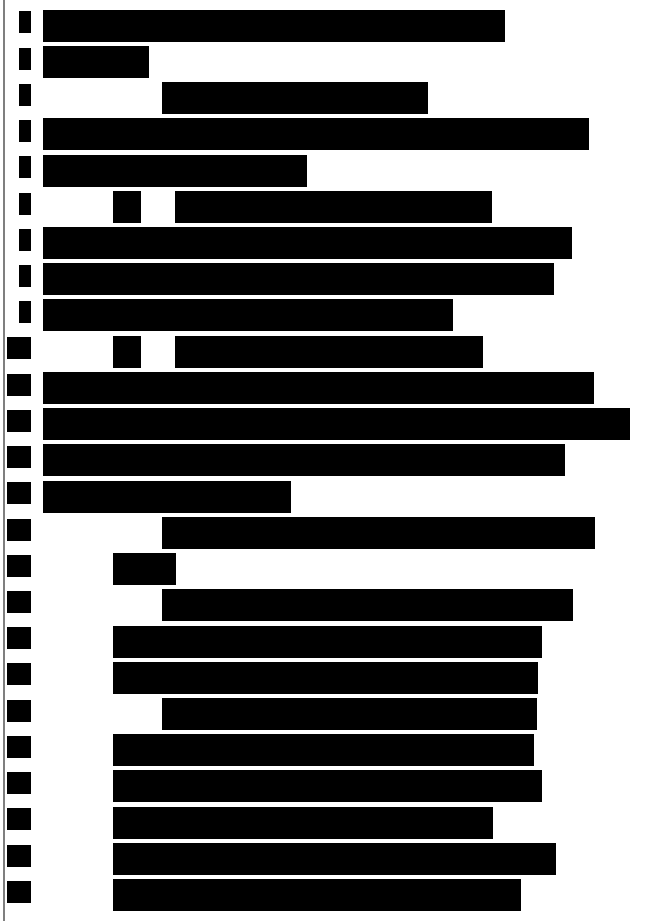

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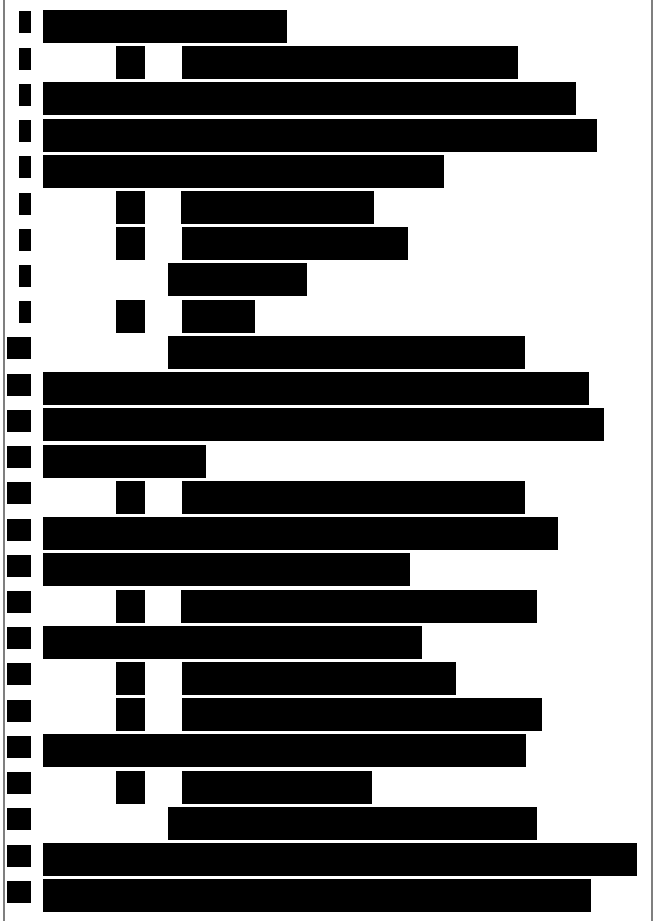

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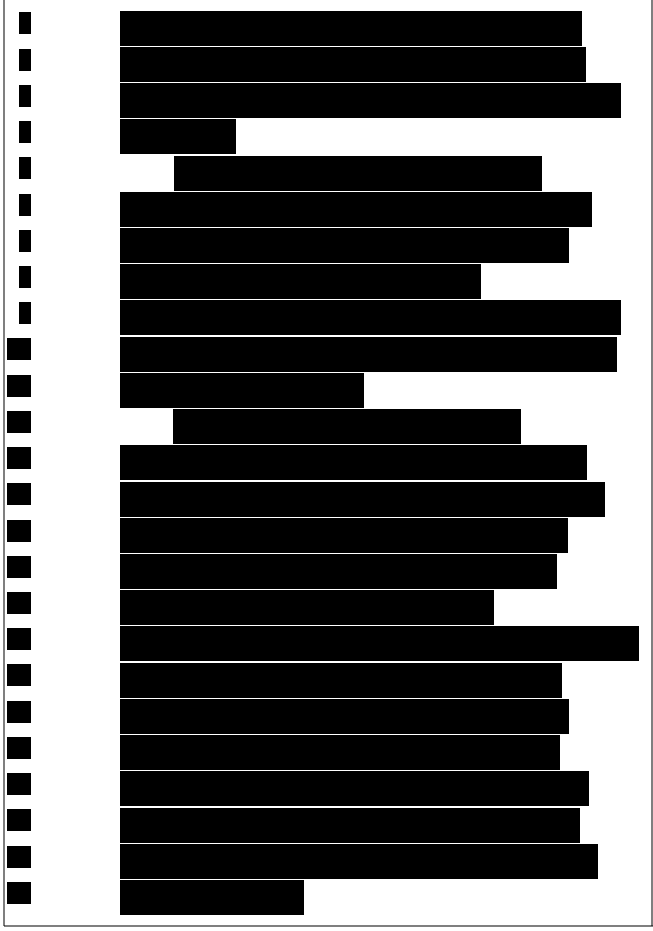

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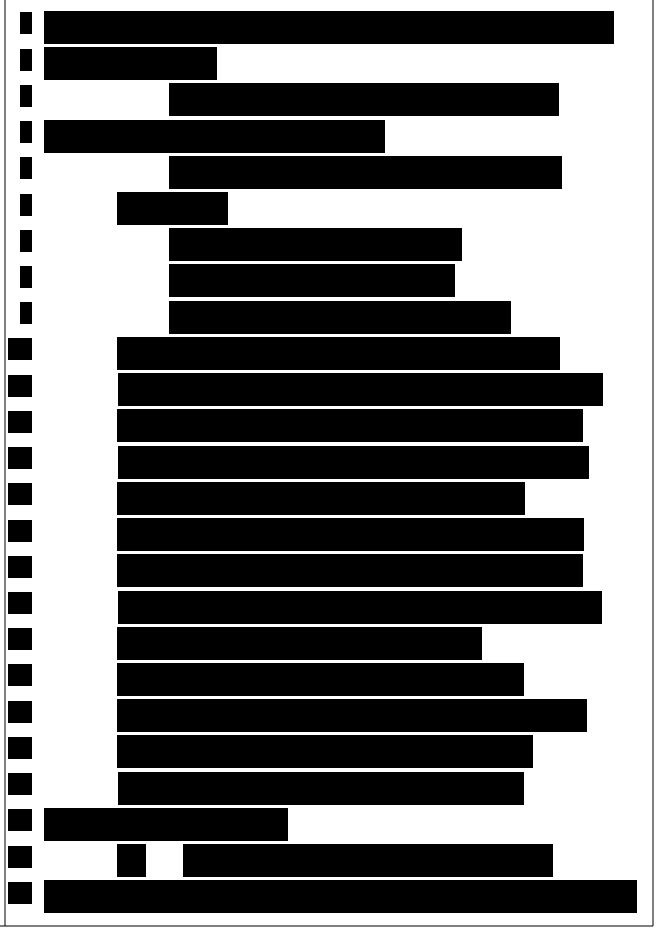

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Q. Thank you, Doctor.

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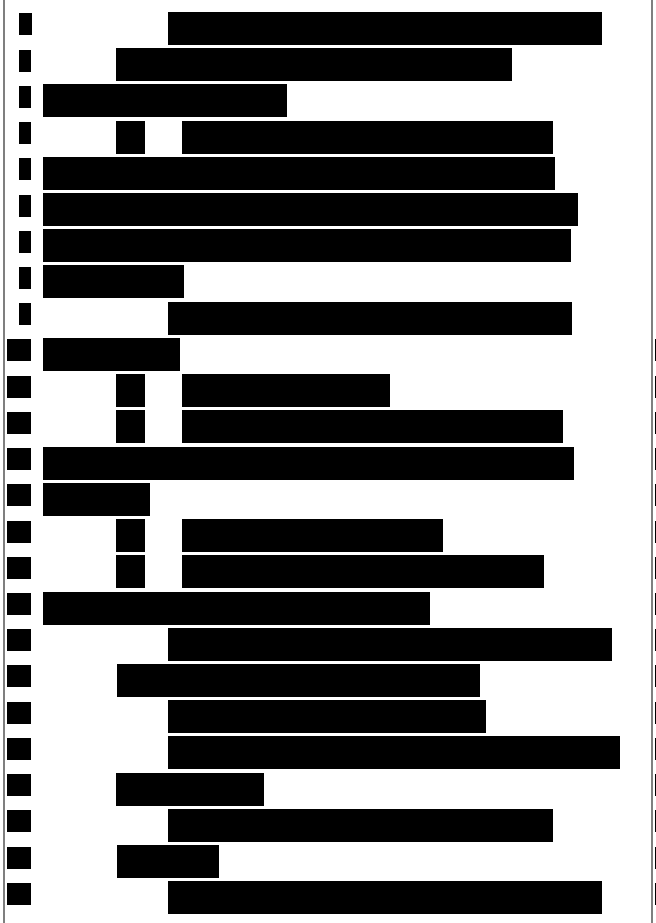

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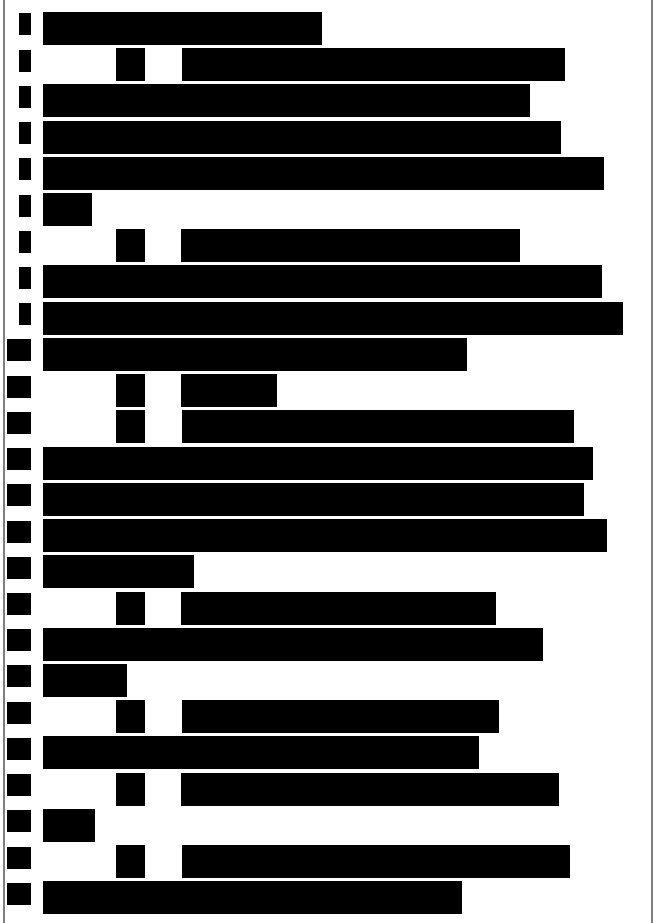

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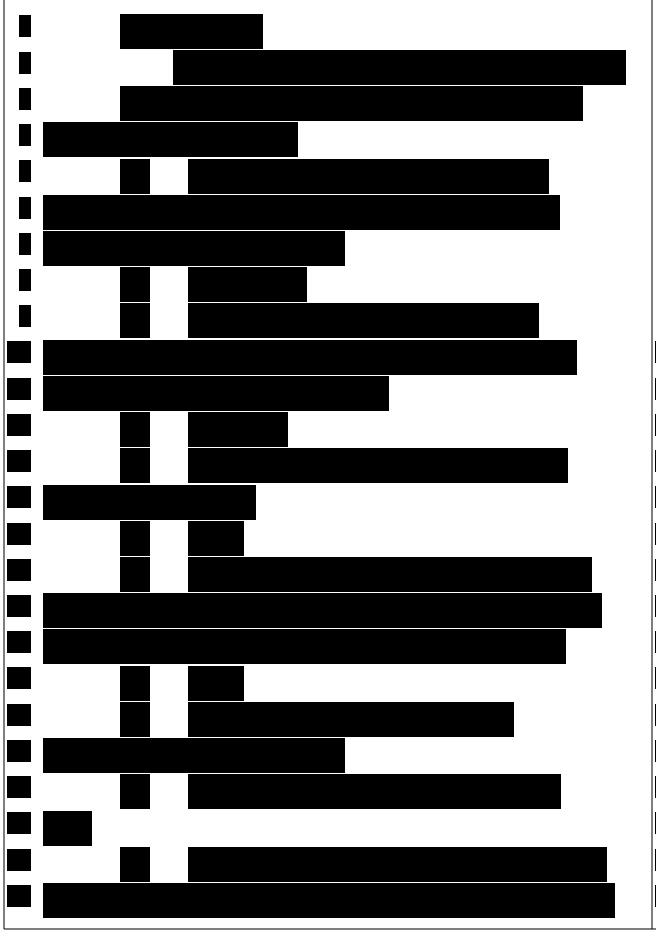

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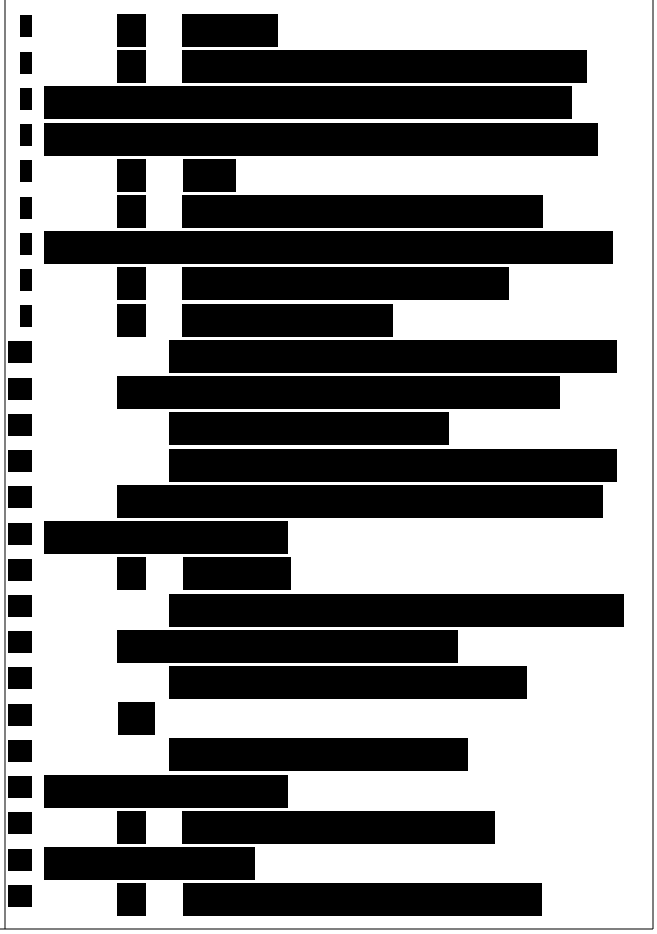

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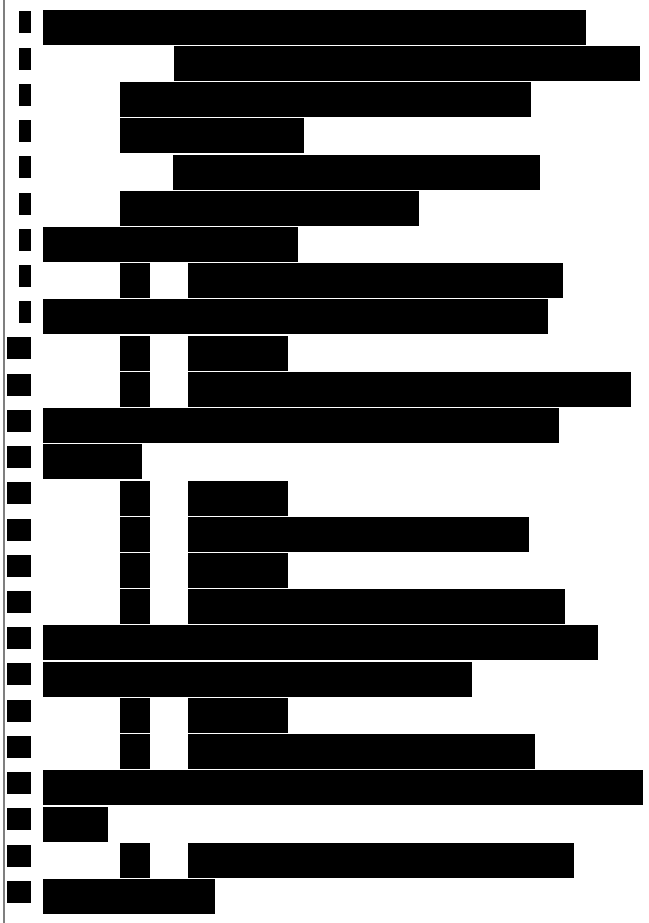

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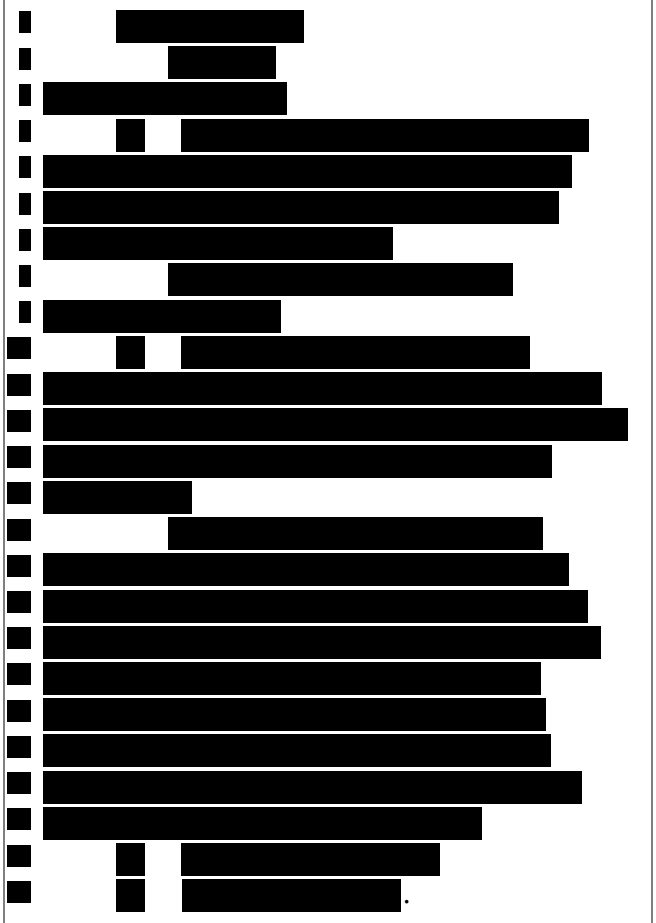

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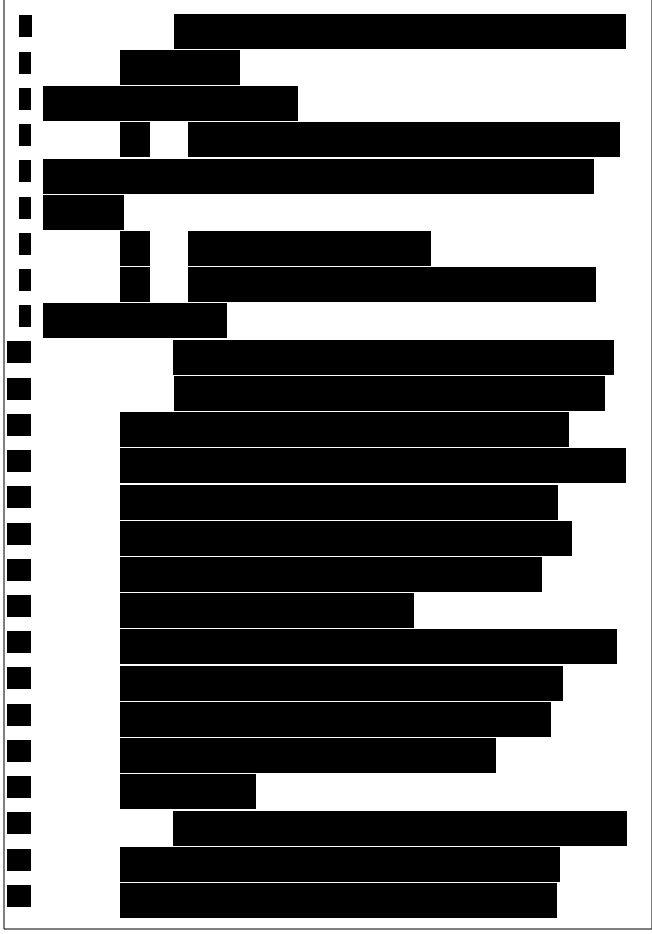

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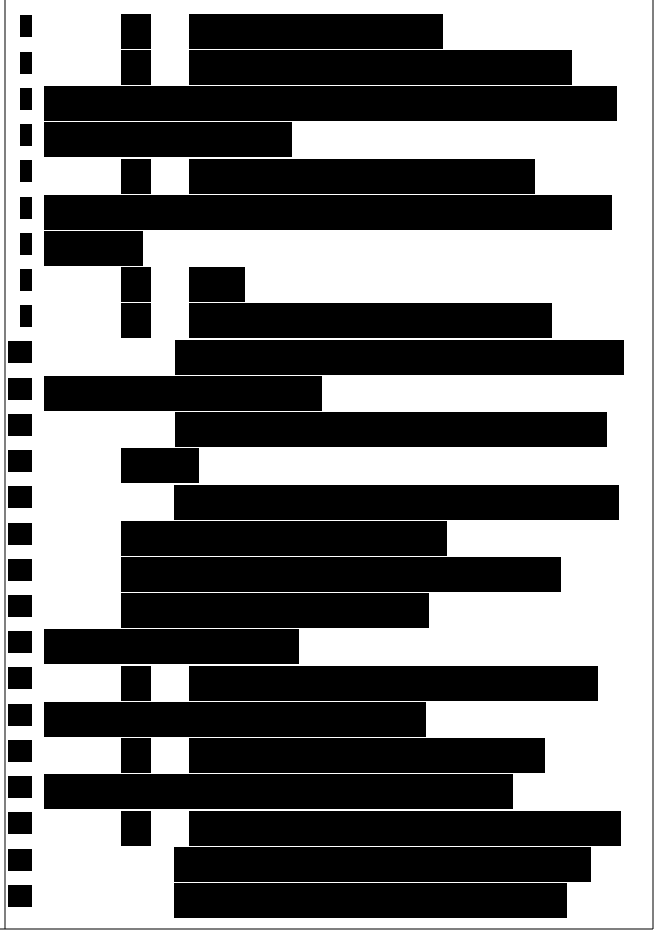

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Q. All right.

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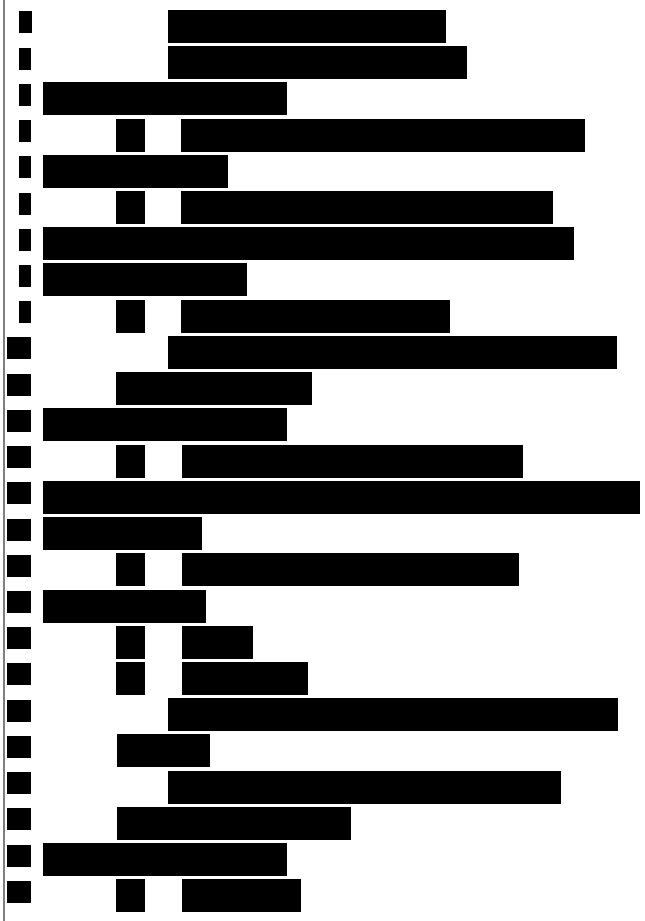

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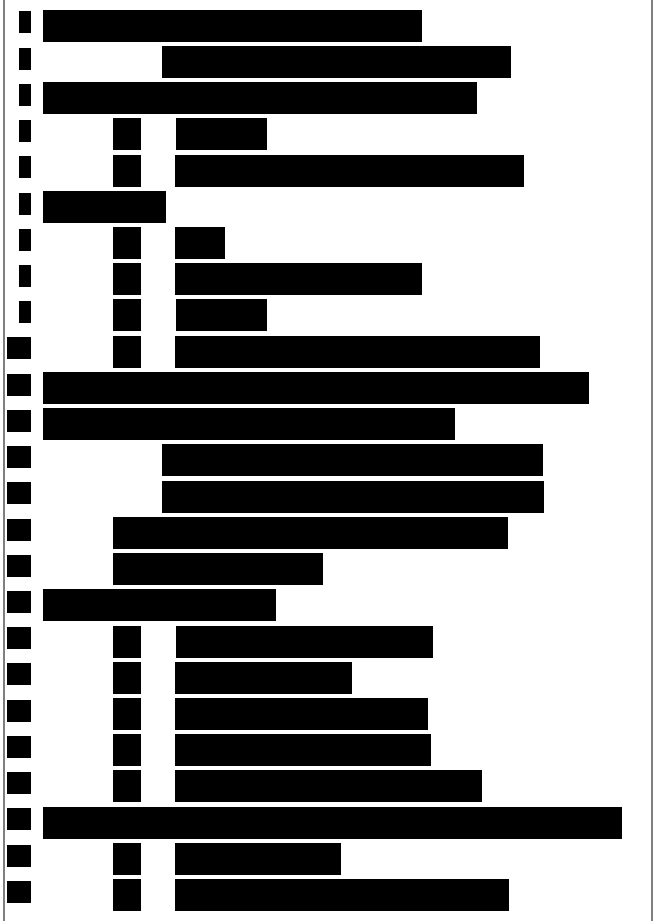

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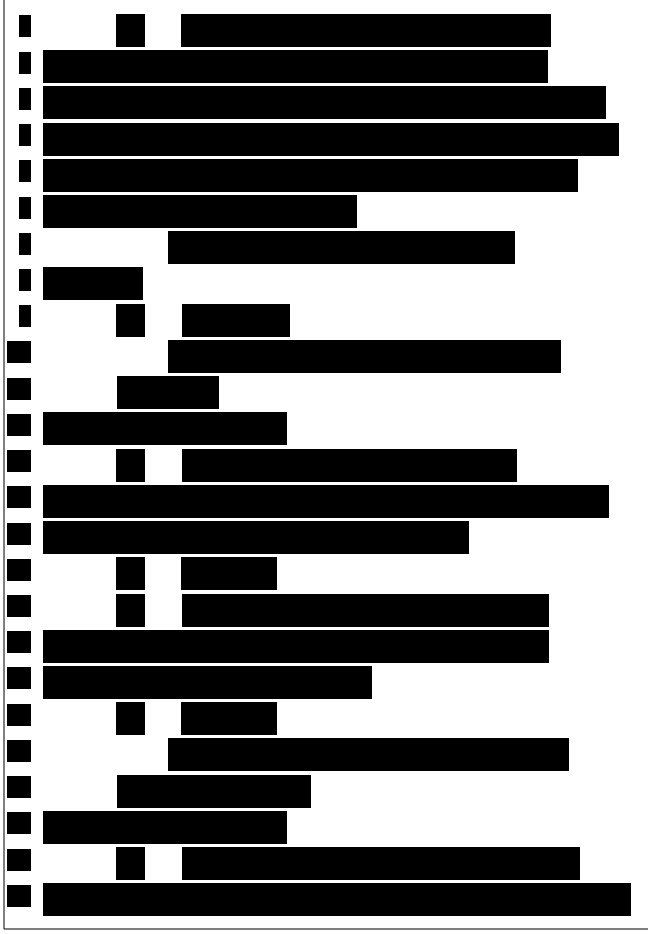

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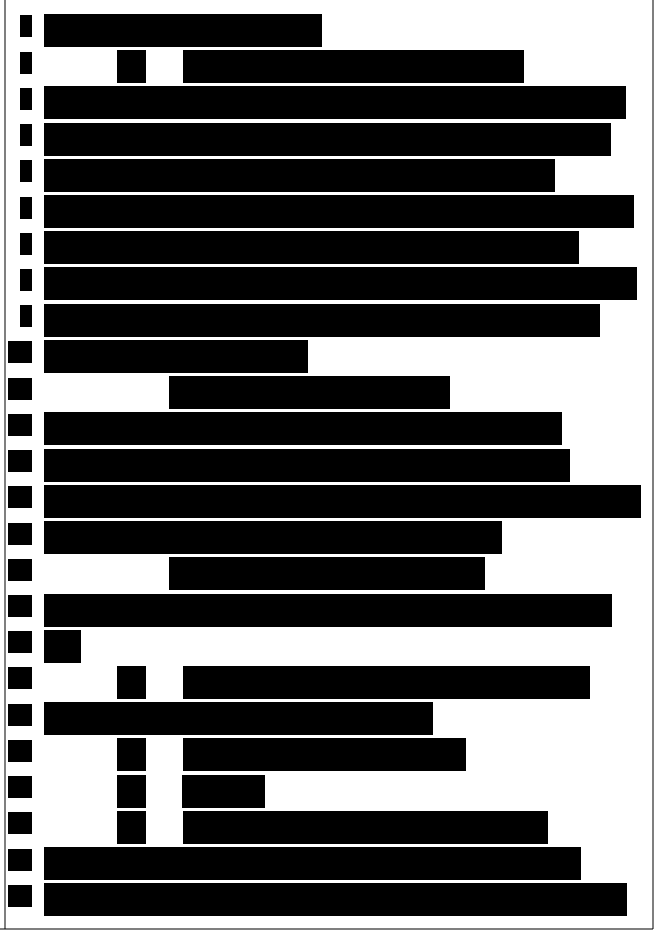

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MR. VAUGHN: Let's go to RO-MDL-2875-0026534.

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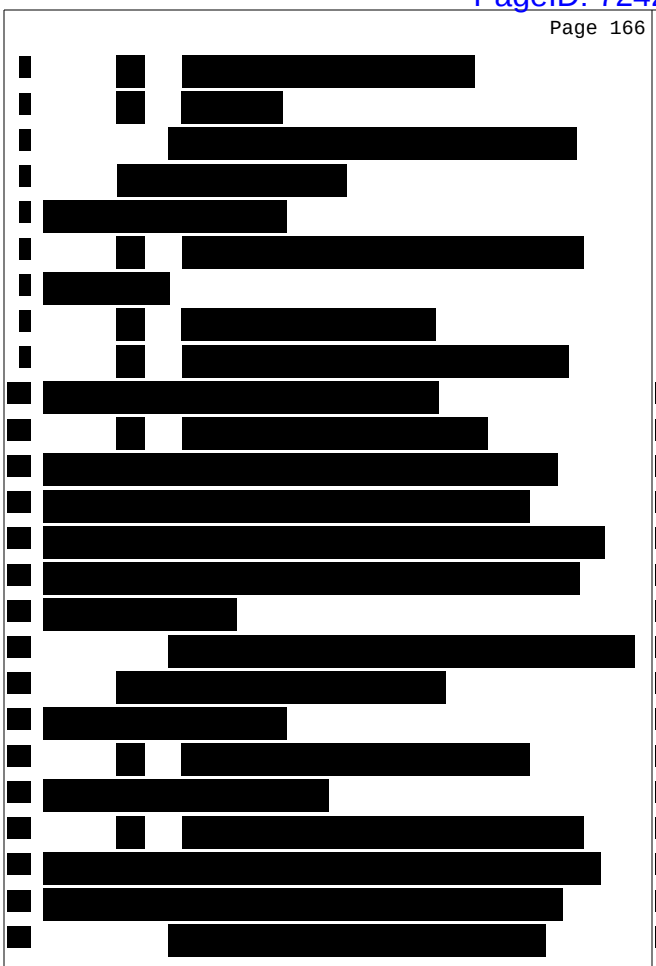

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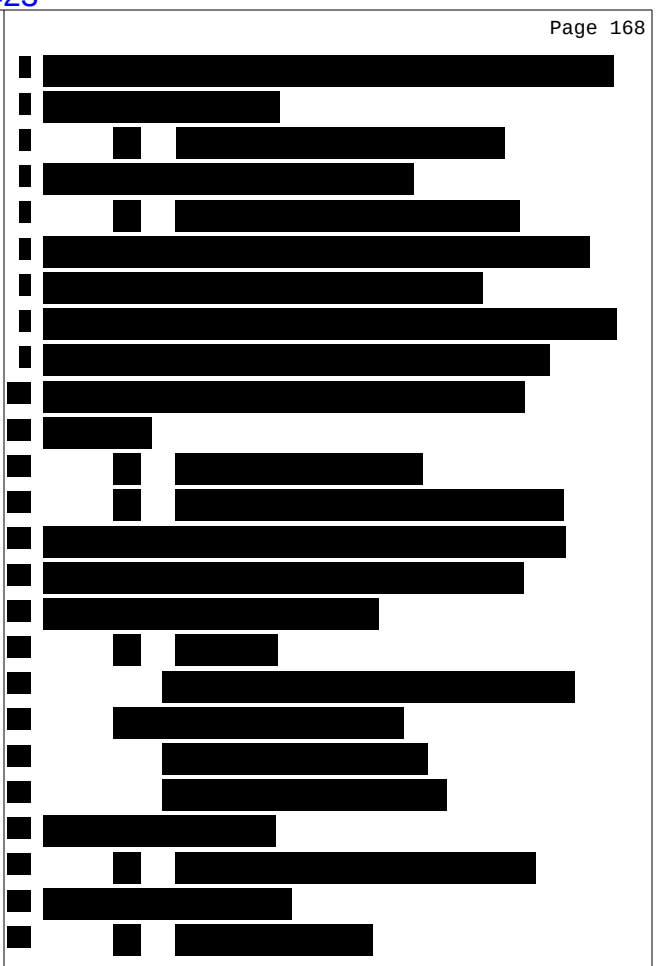

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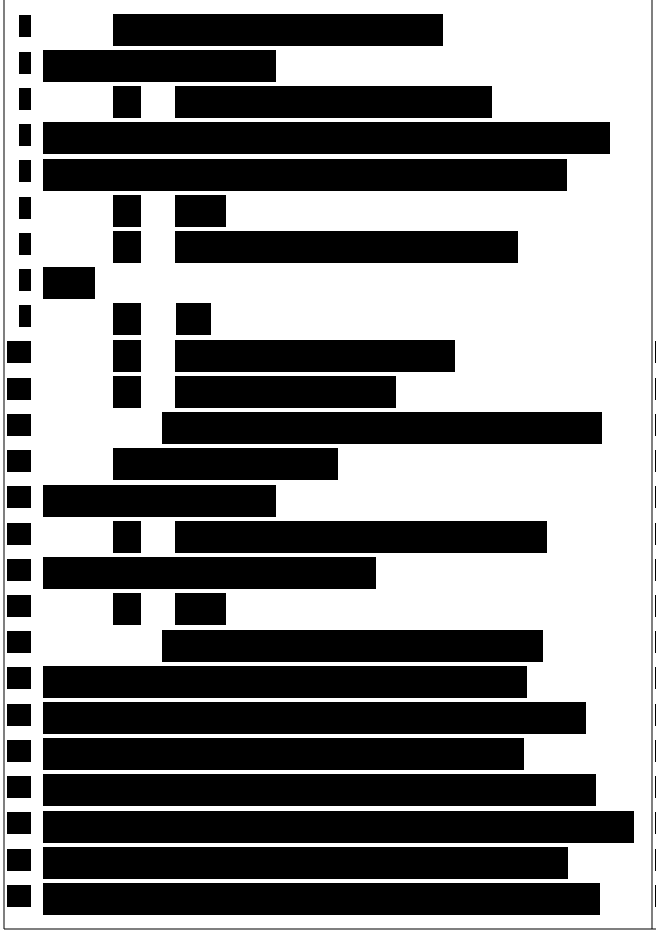

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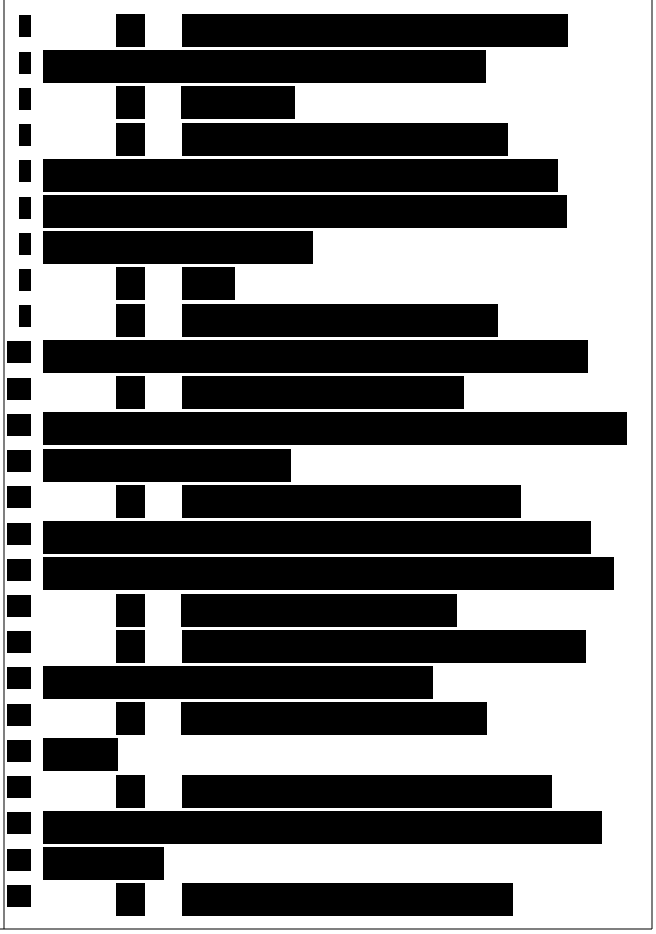

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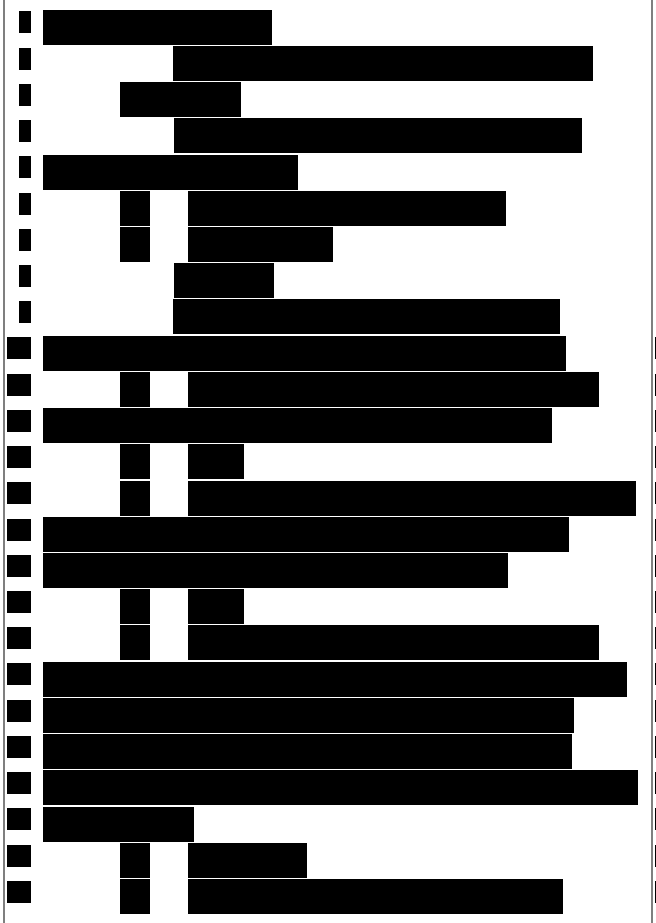

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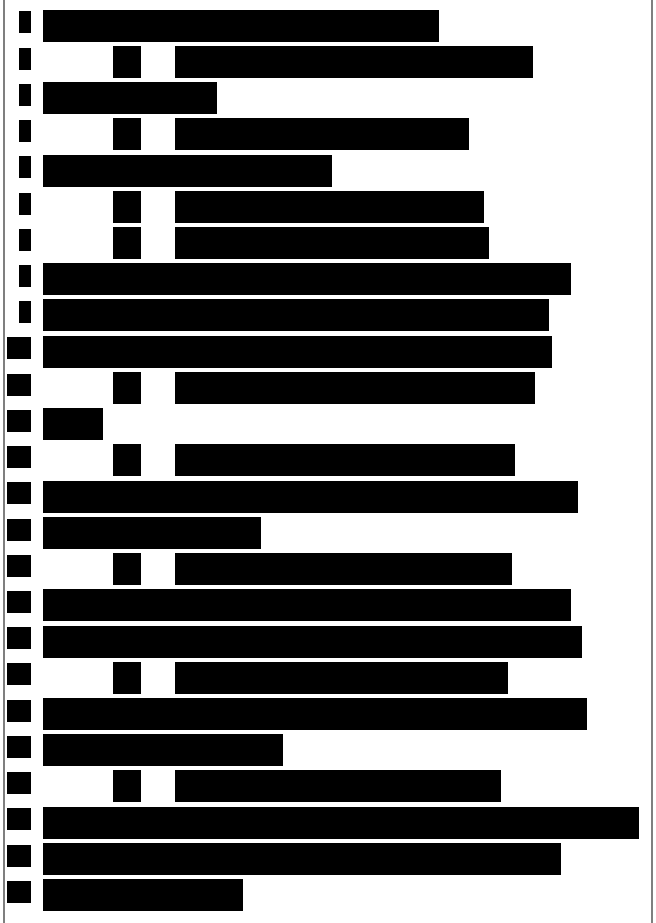

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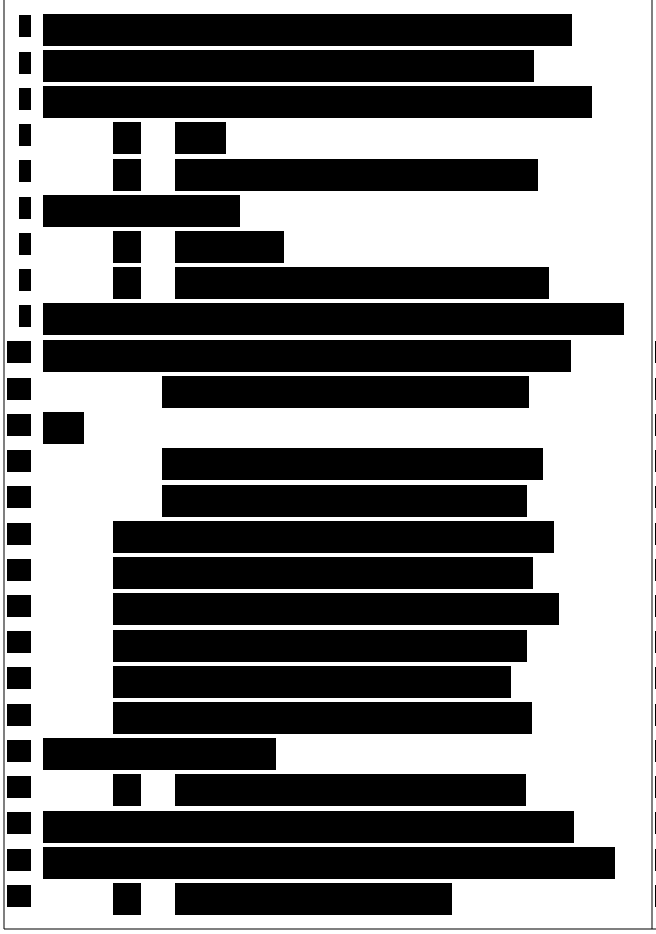

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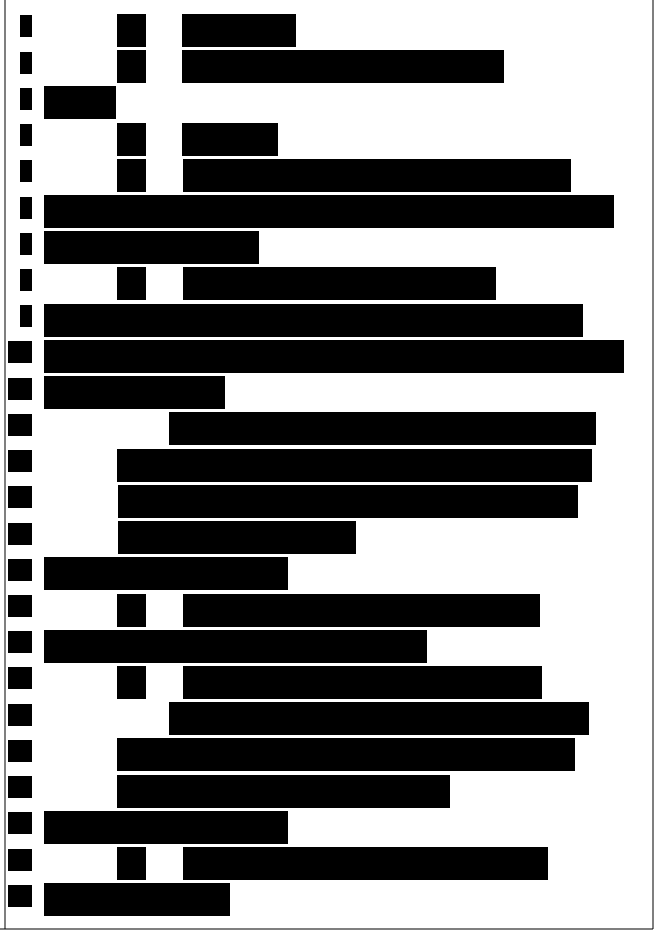

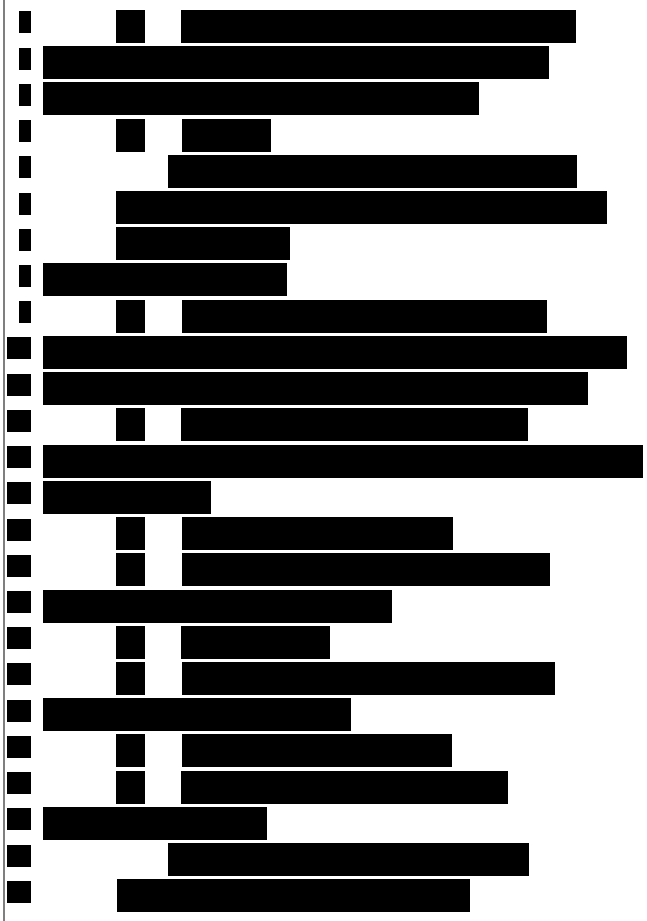

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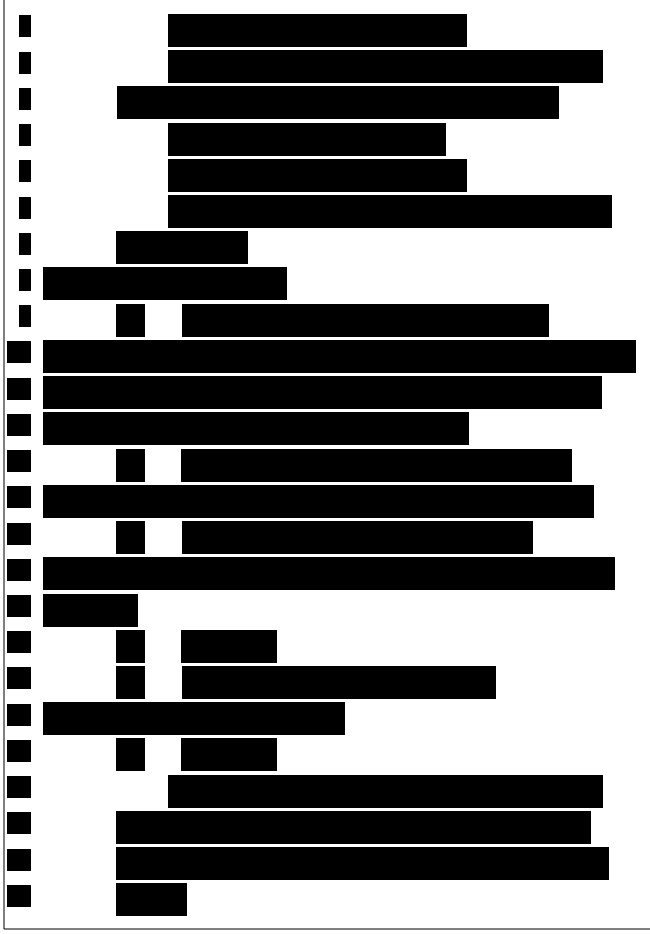

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This will be Exhibit 19.
(Exhibit 19 was marked.)
MR. VAUGHN: And if we can scroll down a little bit -- it's about two-thirds of the way down.
BY MR. VAUGHN:
Q. Doctor, do you see where it says: The pieces of the company, left after bankruptcy, did business as PRACS and returned to the name and the home of one of the legacy companies that had formed Cetero, C-e-t-e-r-o.
Have you ever heard of Cetero before?
A. I'm not sure.
Q. If I represent to you that Cetero is who acquired PRACS, do you have any reason to disagree with that?
A. No I have no reason to disagree with that. Like I said, I thought they were bought out or relocated or something. But that's about all I knew.
MR. FOWLER: Let me object to relevance of this document and line of questioning.
MR. VAUGHN: I'll make it

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relevant real quick for you.
Let's go to the FD- -- the FDA letter to Cetero Research, Melisha.
This will be Exhibit 20.
(Exhibit 20 was marked.)
BY MR. VAUGHN:
Q. All right. Doctor, you see this is a letter from the FDA to Cetero Research?
A. I see that.
MR. FOWLER: I'm going to object to the document and any hearsay contained in the document.
BY MR. VAUGHN:
Q. Have you ever seen this document before, Doctor?
A. No.
Q. All right. That first paragraph towards the bottom, do you see where it says: FDA investigators have identified significant violations of the bioavailability and bioequivalence requirements of Title 21 Code of Federal Regulations Part 320?
A. I see that.
Q. Do you see where the FDA goes on to say that these violations include widespread

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falsification of dates and times in laboratory records and subject sample extractions and the apparent manipulation of equilibrium samples to meet predetermined accepted criteria?

MR. FOWLER: Objection: Hearsay, relevance to anything we're talking about here.

THE WITNESS: Yeah, I see that.

MR. VAUGHN: All right. Let's go to the next page, Melisha. All right. Second paragraph, the last sentence.

BY MR. VAUGHN:

Q. Do you see where the FDA says: "The Complainant was aware that many of the chemists were manipulating and falsifying data associated with the samples being used within various projects"?

MR. FOWLER: Hearsay. A double layer of hearsay.

THE WITNESS: I see that.

MR. VAUGHN: Let's go to page 5, Melisha.

BY MR. VAUGHN:

Q. All right. That first paragraph under No. 2, do you see where they are -- the FDA

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notes that there were frequent alterations in laboratory records that occurred over a four-year period from April 1st, 2005 through June 15th, 2009?

MR. FOWLER: Objection: Facts not in evidence, hearsay.

THE WITNESS: I see it.

BY MR. VAUGHN:

Q. And do you recall the previous bioequivalency studies that we looked at from Mylan were within this date range?

A. They were within that date range.

Q. And the company conducting their bioequivalency studies is the company that the FDA is saying has frequent alterations in their laboratory records?

MR. FOWLER: Objection: Form, hearsay, facts not in evidence.

THE WITNESS: Yeah, I don't see which studies it applies to, but I see that.

BY MR. VAUGHN:

Q. All right.

MR. VAUGHN: Let's go down to the fourth paragraph, three lines up from

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the bottom.

BY MR. VAUGHN:

Q. Do you see where the FDA says that this calls into question the validity of all of the information documented on your AP sheets including study results that were used as a basis for NDAs and ANDAs submitted to the FDA?

MR. FOWLER: Form, relevance, hearsay.

THE WITNESS: I mean, yes, I see that.

MR. VAUGHN: And let's go to the next page, Melisha.

BY MR. VAUGHN:

Q. And under the heading Manipulation of Samples, do you see where it says: "FDA has determined that your firm manipulated test samples in order to meet predetermined acceptance criteria"?

MR. FOWLER: Form, lack of foundation, facts not in evidence, relevance.

THE WITNESS: I see that.

MR. VAUGHN: And let's go to page 10, Melisha.

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BY MR. VAUGHN:

Q. And do you see where the FDA, on the second paragraph, notes they have significant concerns of all data relevant to FDA-regulated research?

A. At the Houston facility, yes.

Q. And --

A. My recollection is we talked about Minneapolis and North Dakota, not Houston.

Q. So it's your opinion that just the Houston office was manipulating data for this company?

MR. FOWLER: Objection: Form, mischaracterizing, lack of foundation, facts not in evidence.

THE WITNESS: It's not my testimony. It's what's in the letter that you just provided me.

MR. VAUGHN: And let's go to page 11, Melisha.

BY MR. VAUGHN:

Q. And this was signed by the FDA's Chief of Bioequivalence Investigations branch, correct?

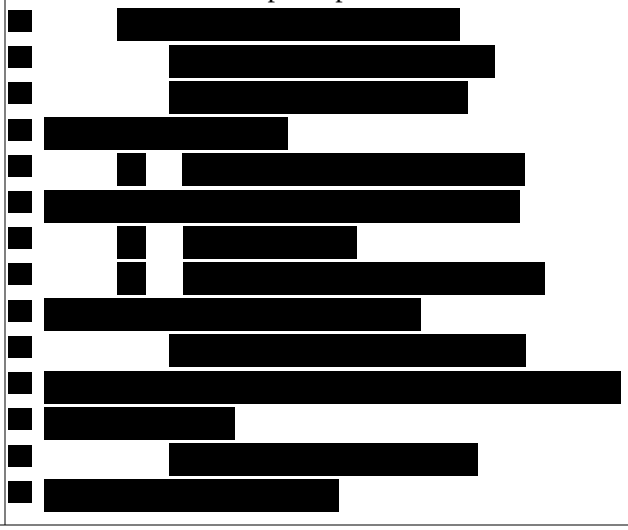
A. Well, I don't see a signature,

but....
Q. The name and the position of the person at the end of the letter is the FDA's Chief of Bioequivalence Investigations branch, correct?
MR. FOWLER: Object to the mischaracterization of that being a signature.
MR. VAUGHN: Oh, you're right.
BY MR. VAUGHN:
Q. Signature is the Office of Scientific Investigations and Office of Compliance for the Centers of Drug Evaluation and Research, U.S. FDA, Food & Drug Administration, correct?
A. Yes, I see the -- the listing of those people's names and their positions there.
MR. VAUGHN: All right, Melisha, let's go to Teva ANDAs Withdrawn over Cetero Data document. Let's go to the second page.
This will be Exhibit 21.
(Exhibit 21 was marked.)
BY MR. VAUGHN:
Q. That top paragraph, Doctor, do you see where it says: After a six-year effort, the U.S. FDA has run out of patience with Watson

Laboratories and InvaGen Pharmaceutics and is moving to withdraw approval of two of their pr- -- abbreviated new drug applications because the firms failed to conduct additional bioequivalency studies for the products the companies' ANDAs were supported by, bioequivalence studies conducted at Cetero Research?
MR. FOWLER: Objection: Hearsay, lack of foundation, facts not in evidence, relevance.
THE WITNESS: I see that.
BY MR. VAUGHN:
Q. Are you aware that Watson is now Teva?
A. I'm aware that -- now how to -- how to -- how to word who's what, but I think they either bought Watson or incorporated Watson or something.
Which -- which ANDAs were withdrawn? Were they the ones I'm talking about or other ANDAs?
Q. They're ANDAs that used the same contract research organization to do their bioequivalency studies.
A. Well, again, the -- the data that

you showed me was concerned about the Houston facility. The ANDAs that I cited were done in North Dakota and Minneapolis, No. 1; and then secondly, it looks like the ANDAs that were withdrawn were not the ones that I reported in -- in my report.
So I think if the FDA had had a problem with those in those other facilities, then they would have withdrawn those like they did these.
Q. And you see here it took the FDA six years before they withdrew it, correct?
MR. FOWLER: Form.
THE WITNESS: I -- I mean, whatever it says, that's what it says, but I'm saying it didn't involve the ANDAs that I reported on.
BY MR. VAUGHN:
Q. But it did involve the contract research organization that did the studies for the ANDAs you reported on, correct?
A. Correct. Except not in the facility that was cited. In the other facilities that was not cited.
Q. My headset just made a noise that

it's low on batteries.
MR. VAUGHN: Can we go off the record real quick, just take a five-minute break?
THE VIDEOGRAPHER: The time is now 2:45 p.m. We're off the record.
(Brief recess observed.)
THE VIDEOGRAPHER: The time is 2:53 p.m. We're back on the record.
MR. VAUGHN: All right, Melisha, can we now pull up



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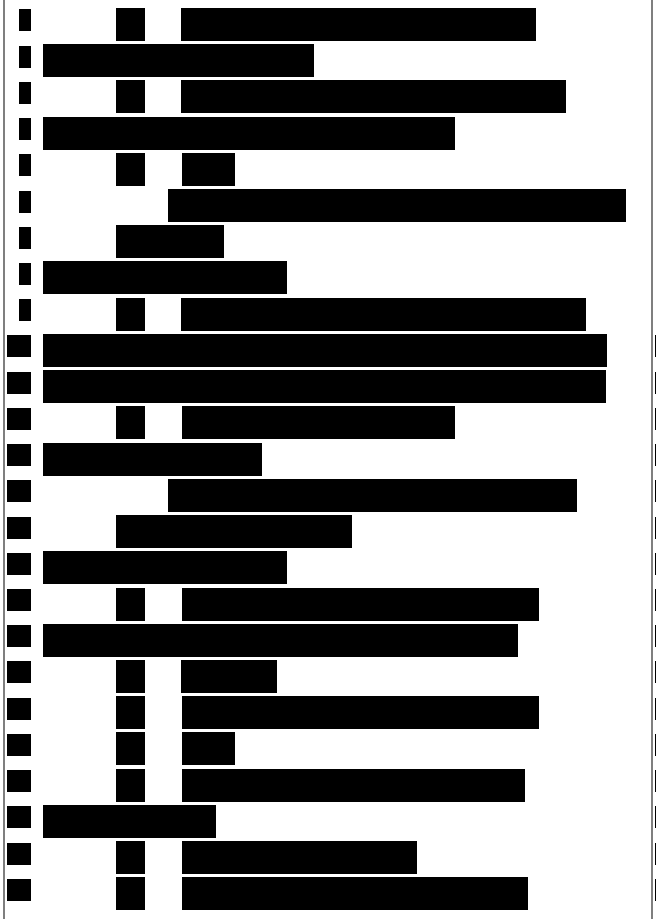

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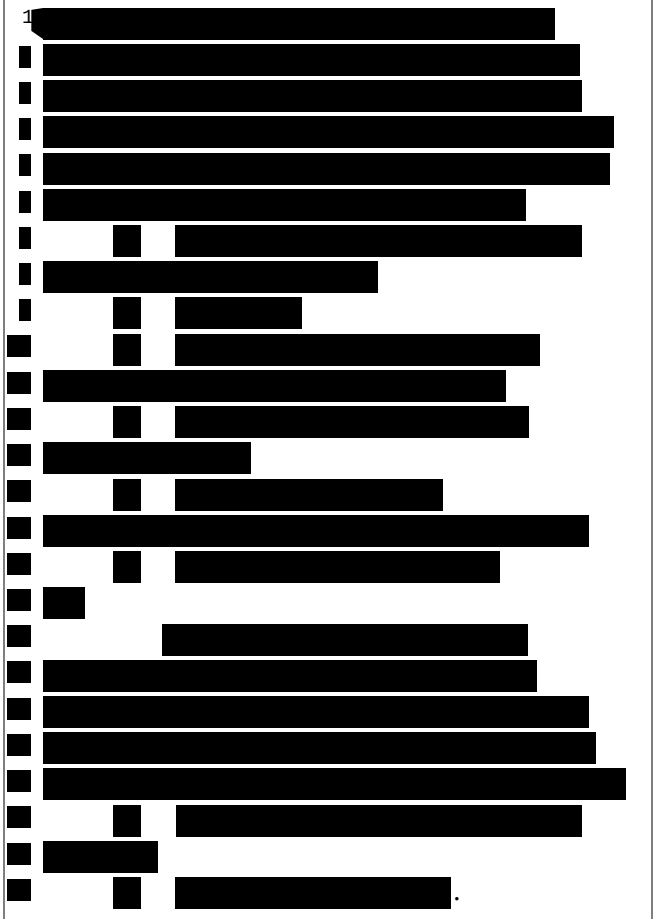

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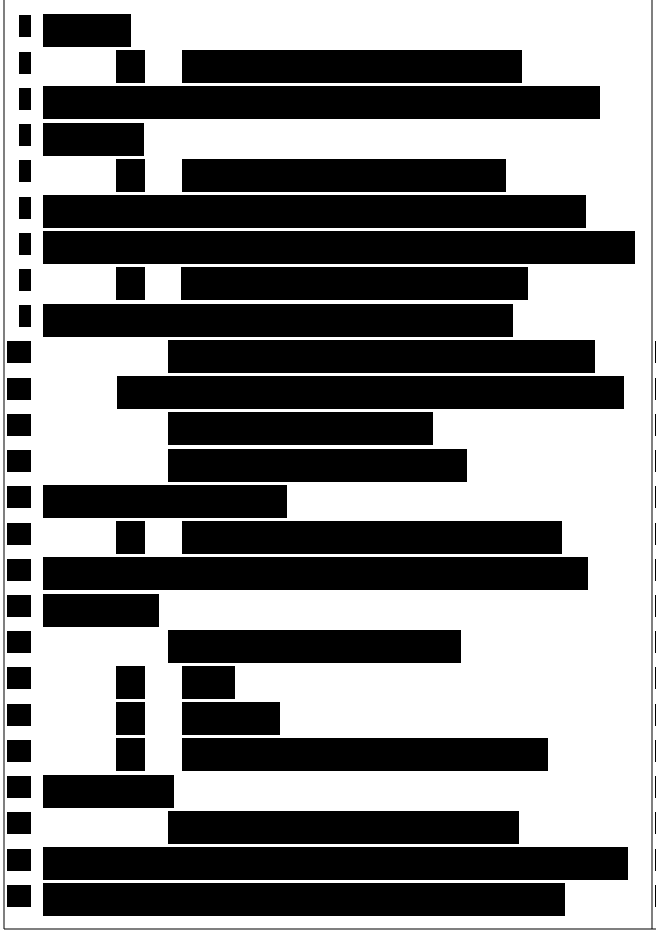

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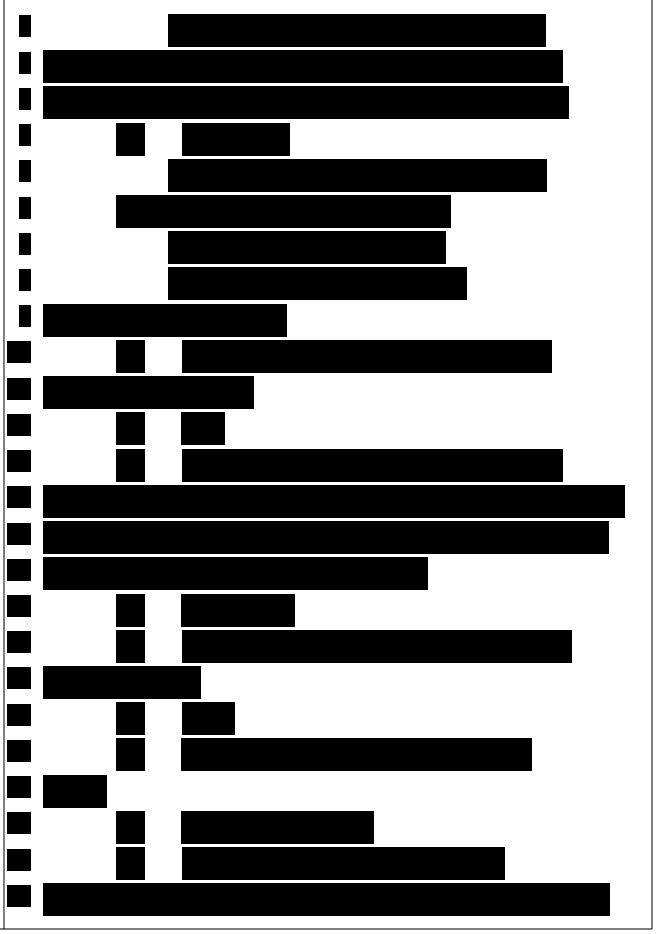

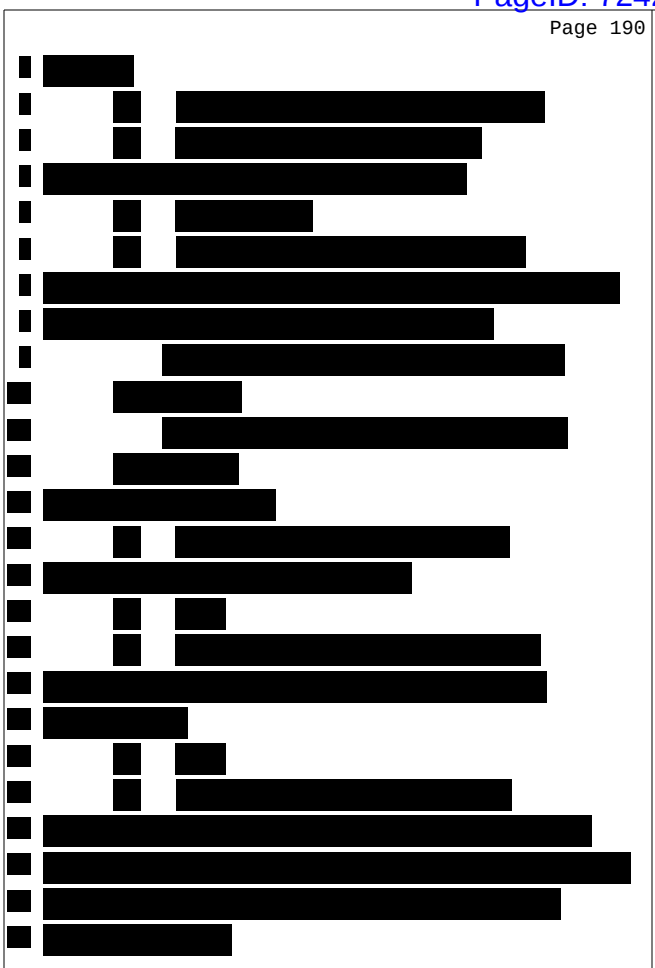

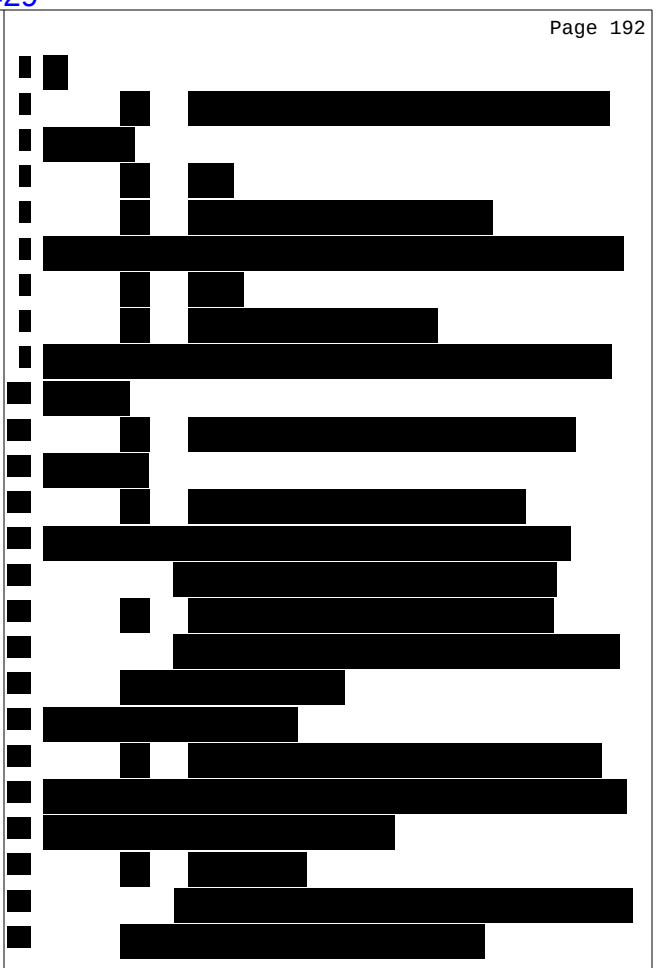

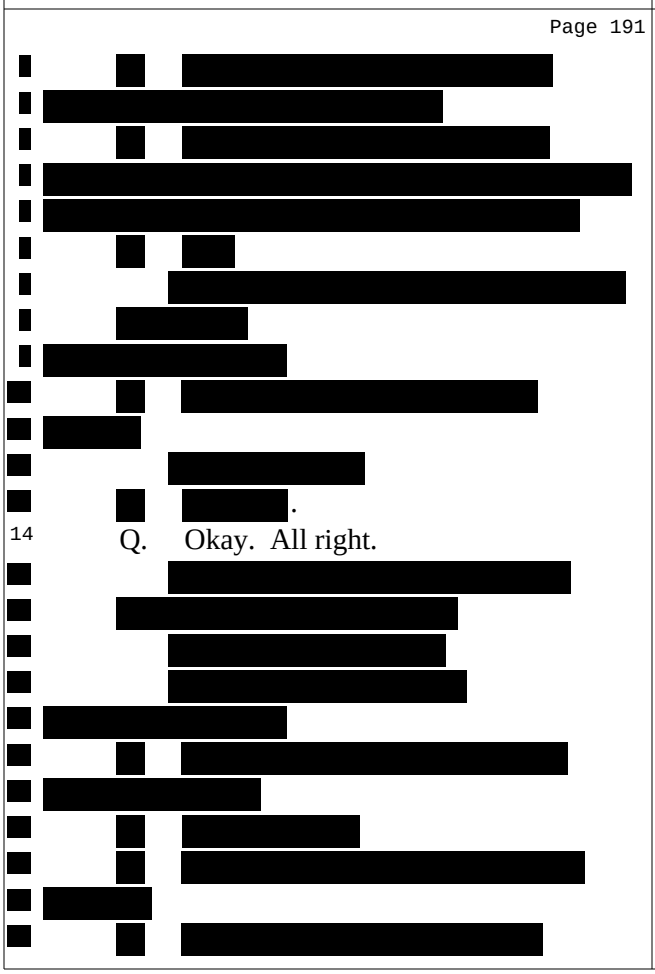

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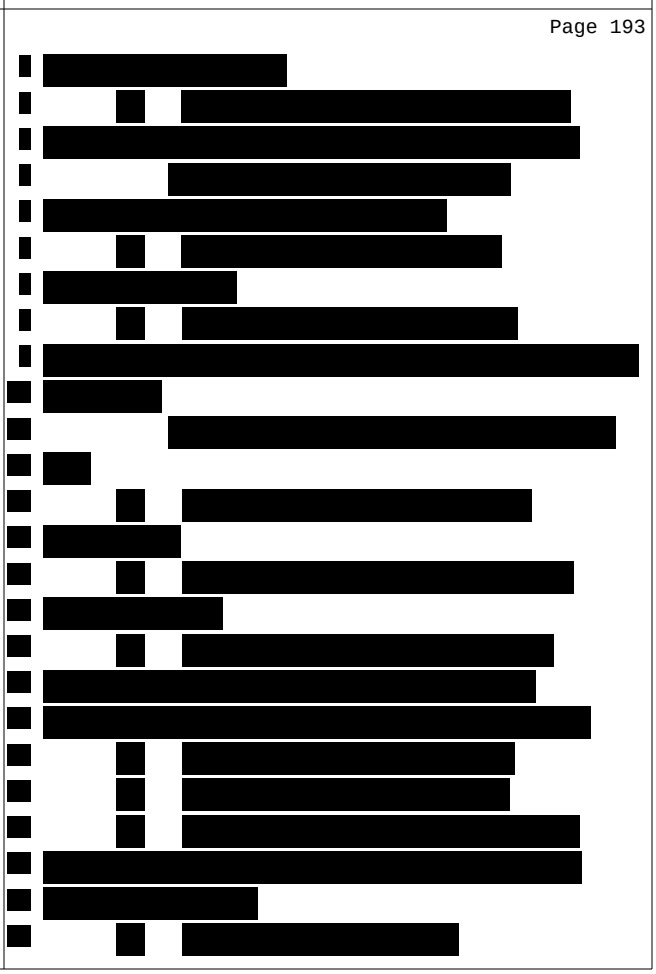
Q. Okay. All right.



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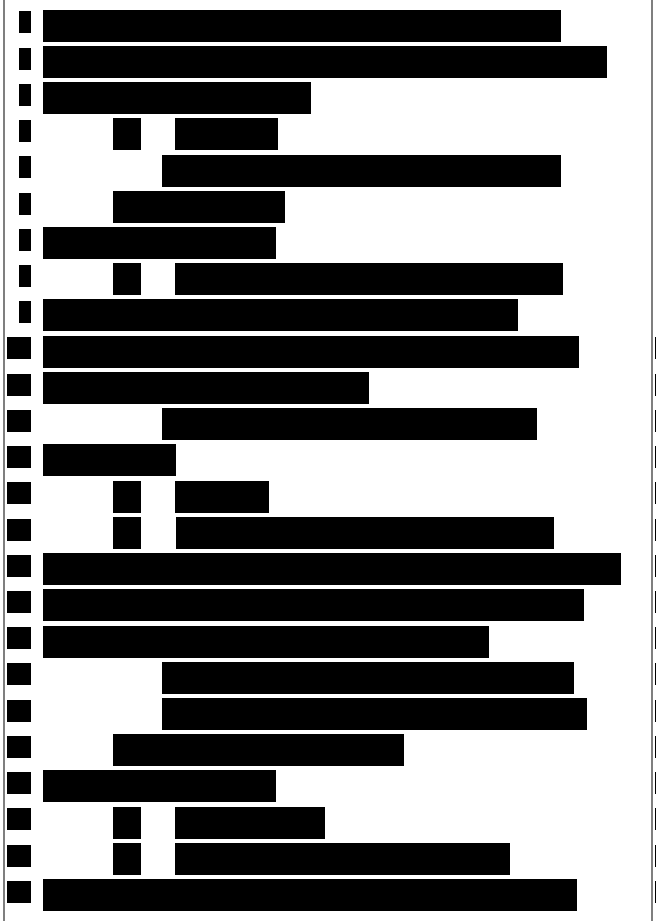

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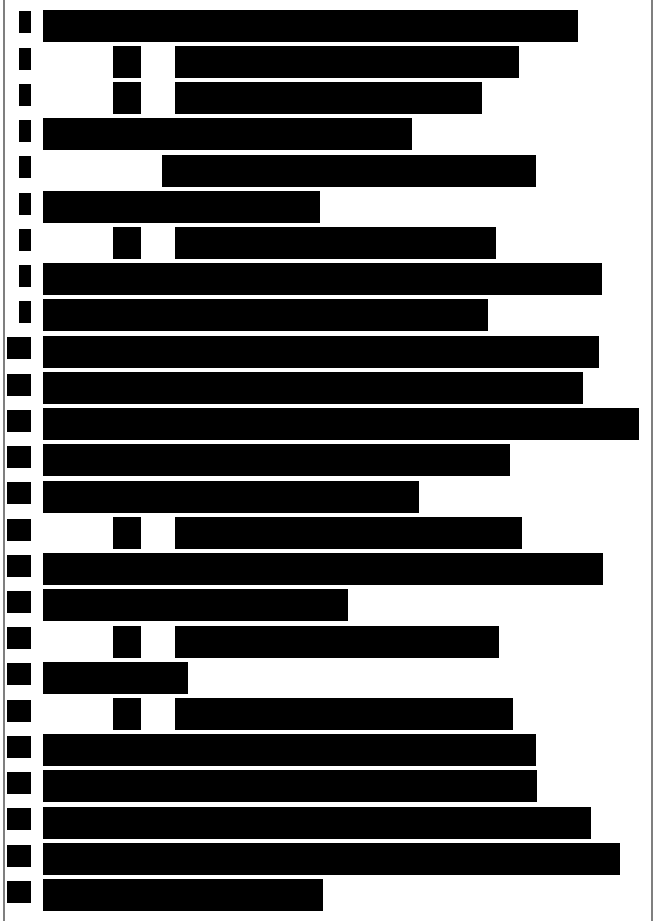

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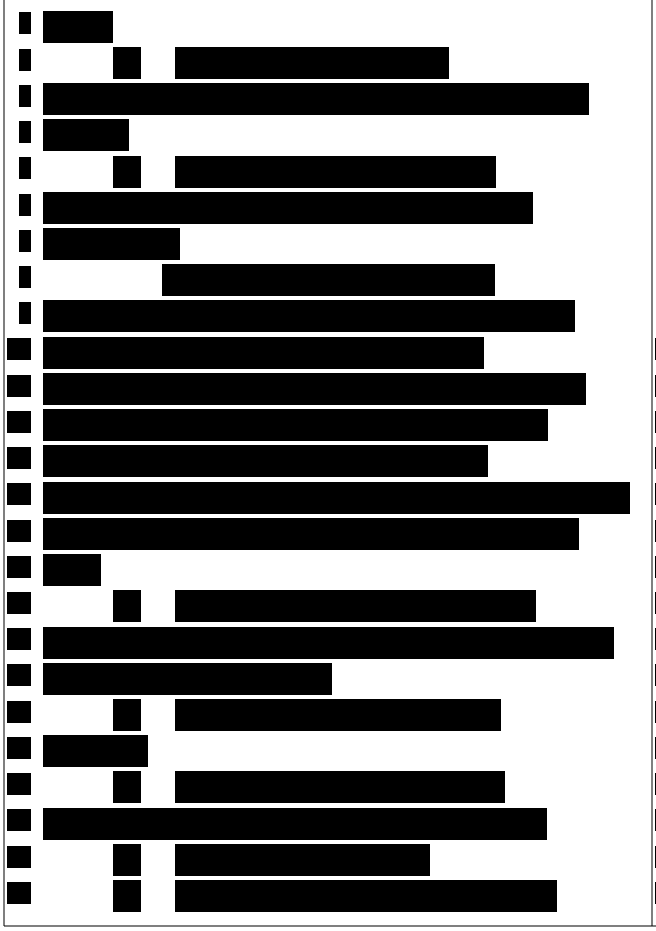

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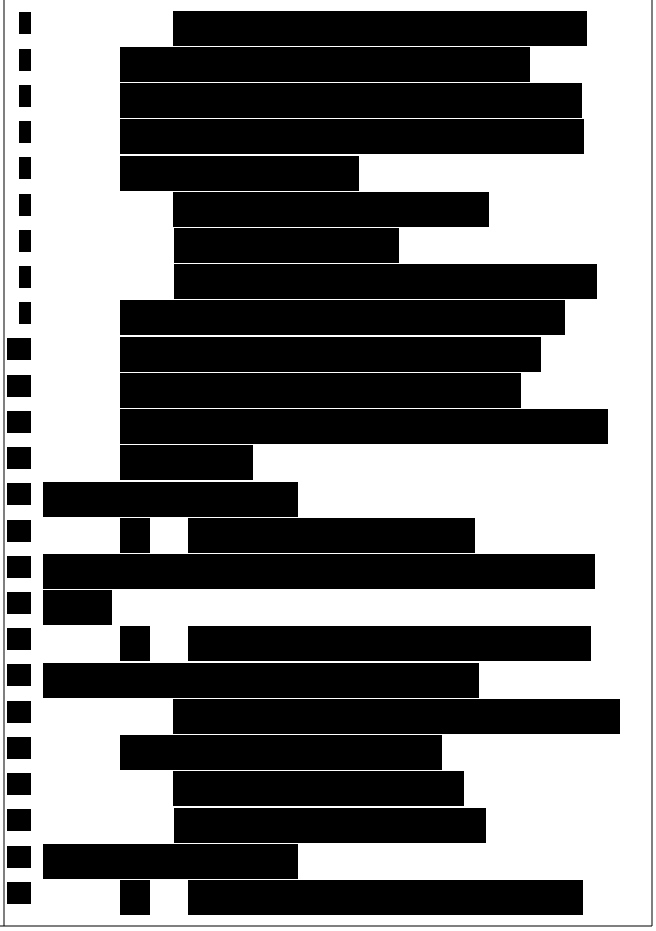
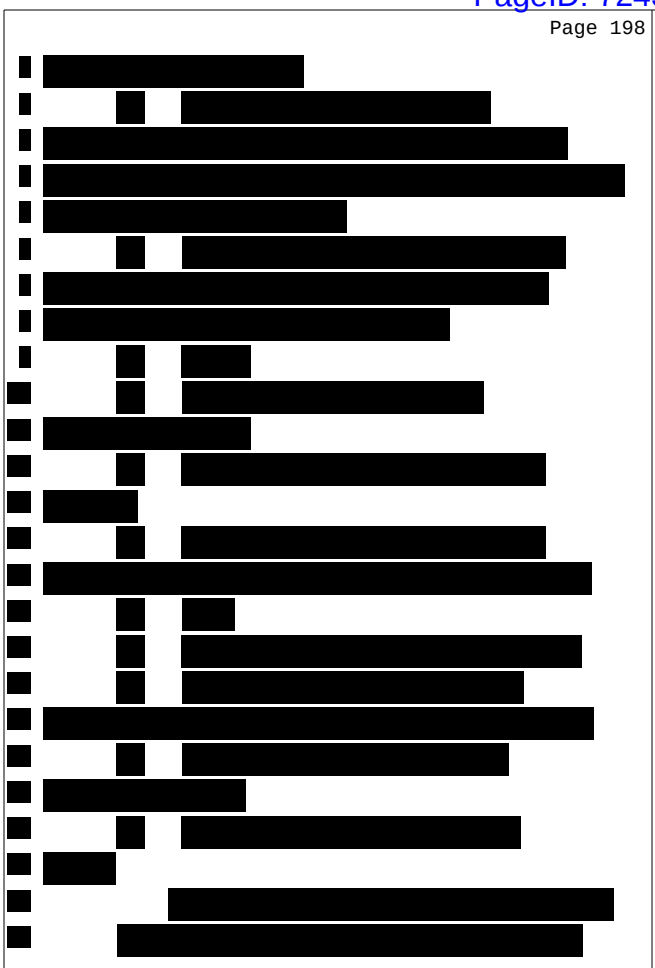
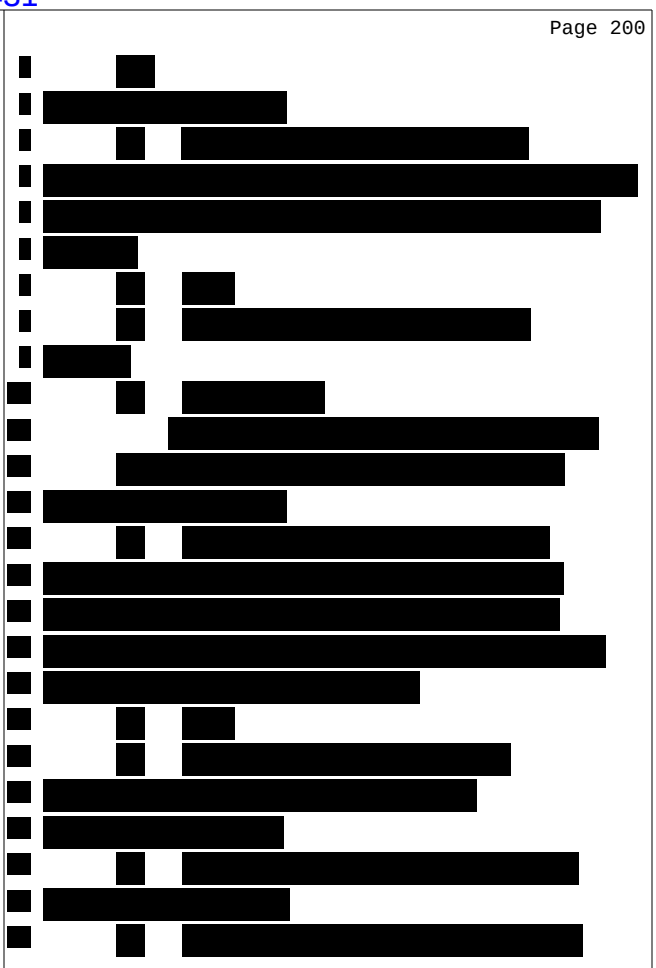
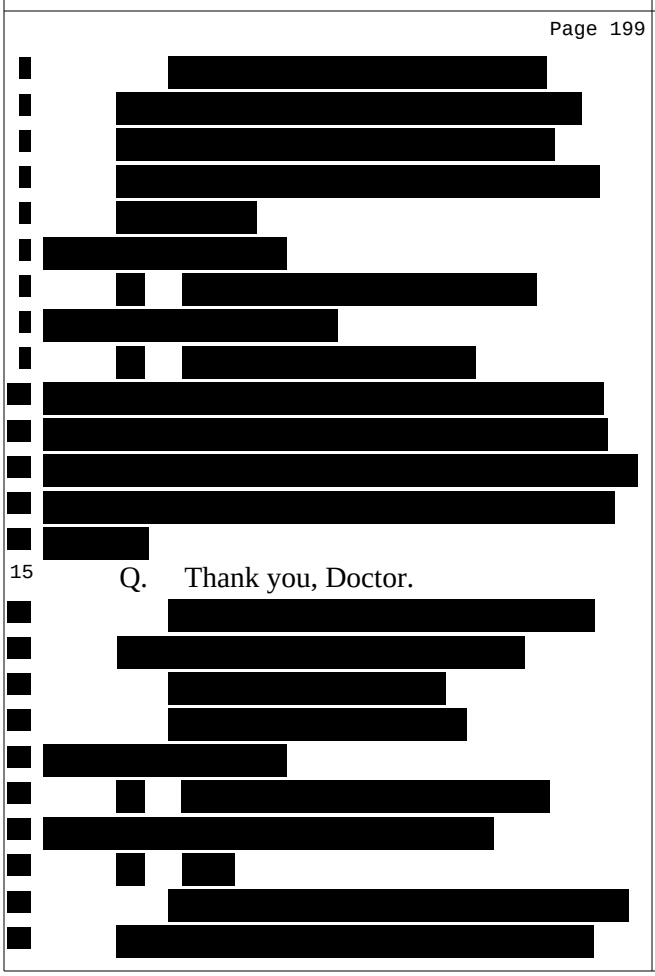
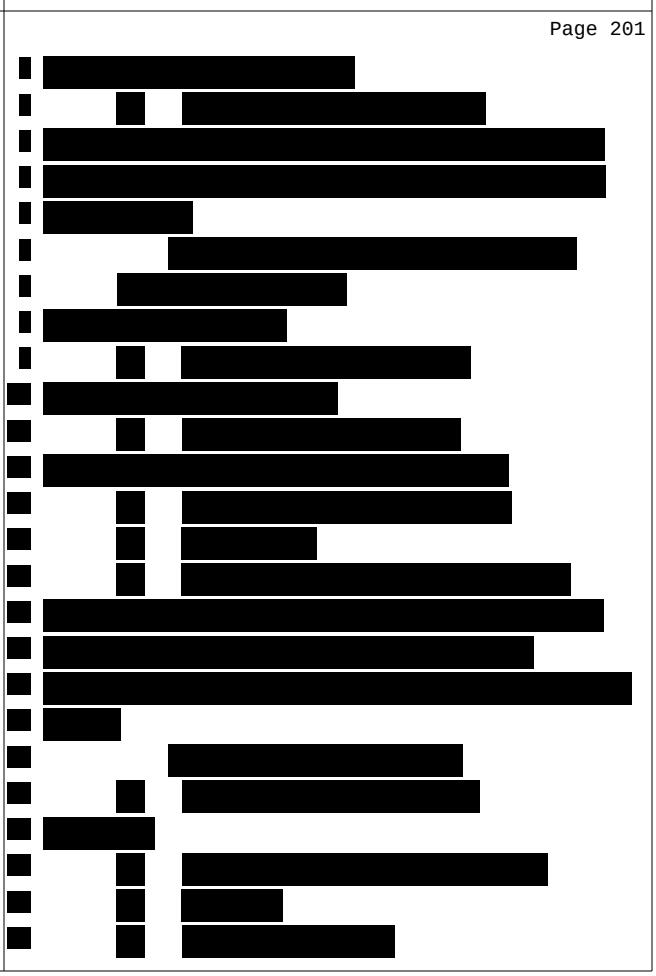








15 Q. Thank you, Doctor.

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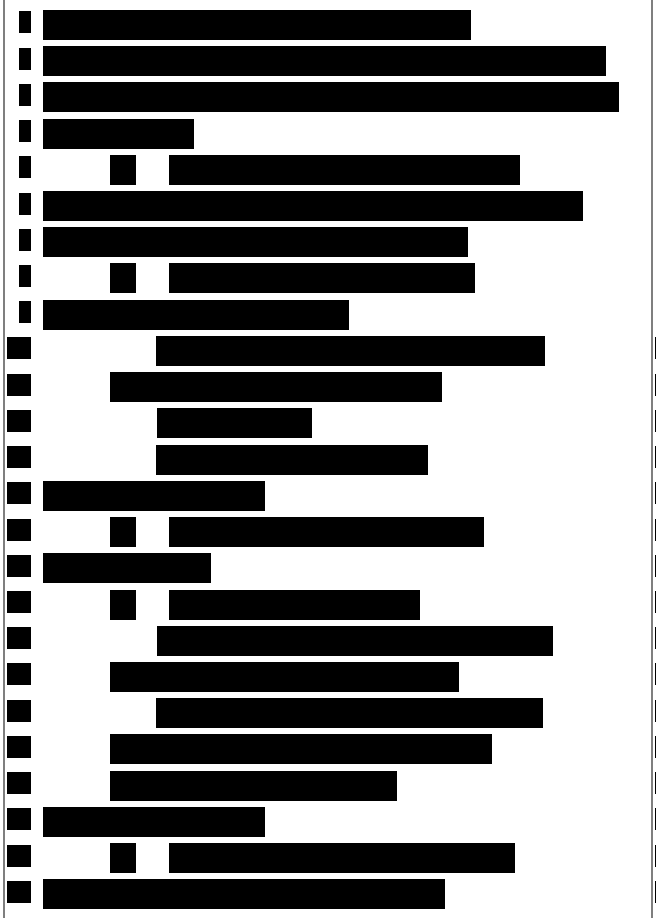

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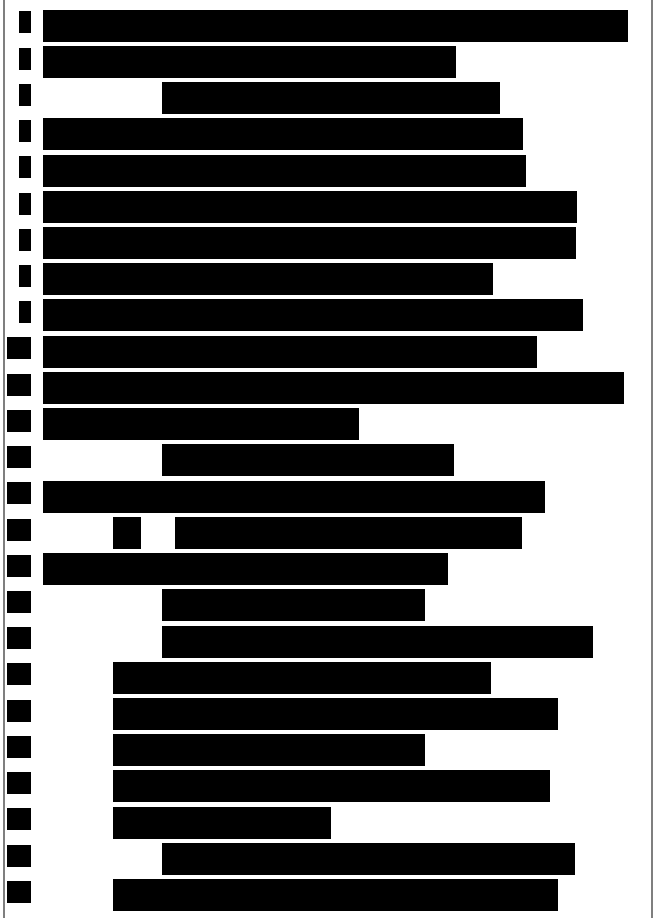

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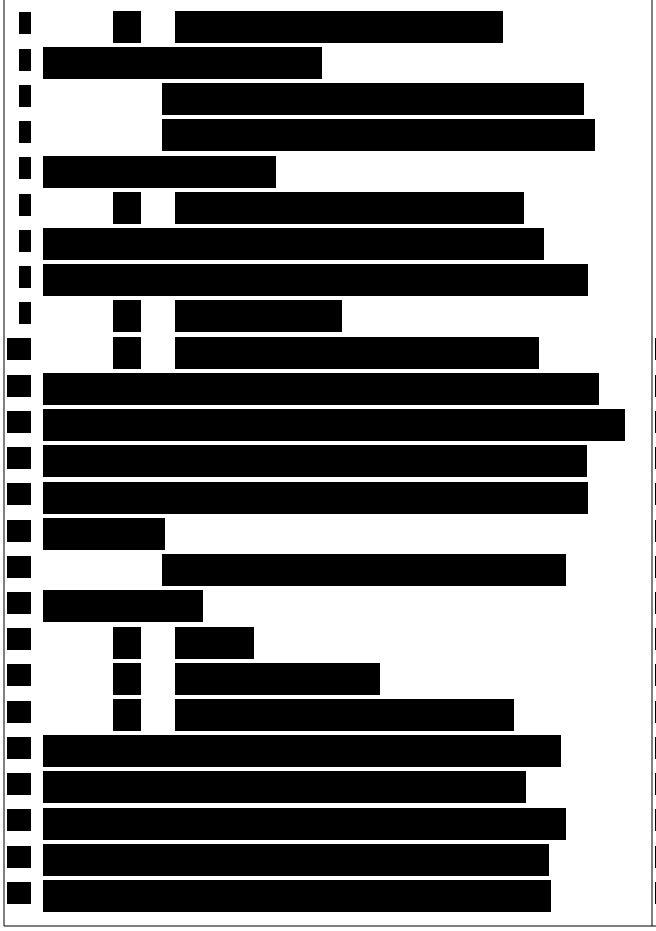

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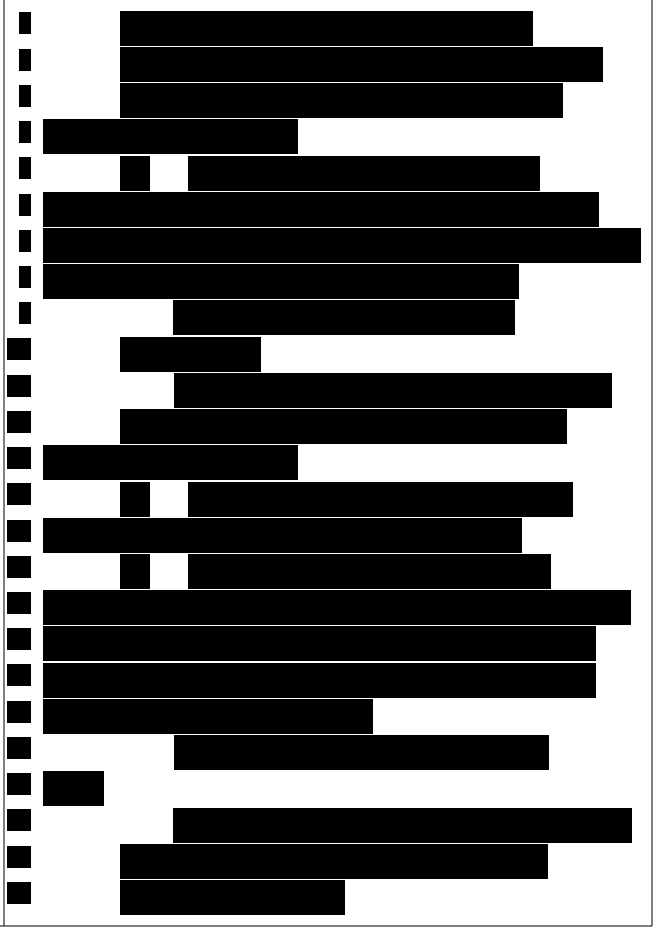

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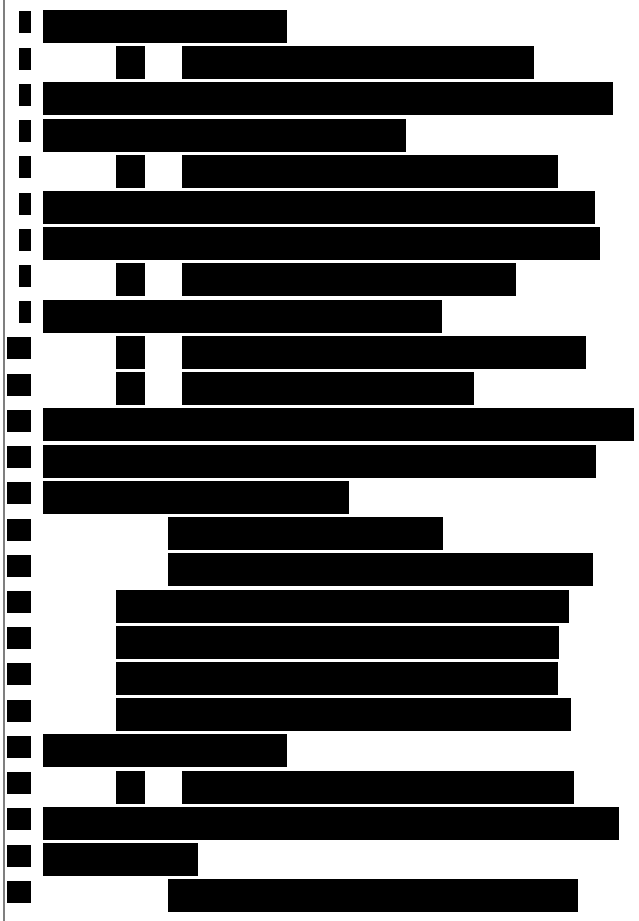

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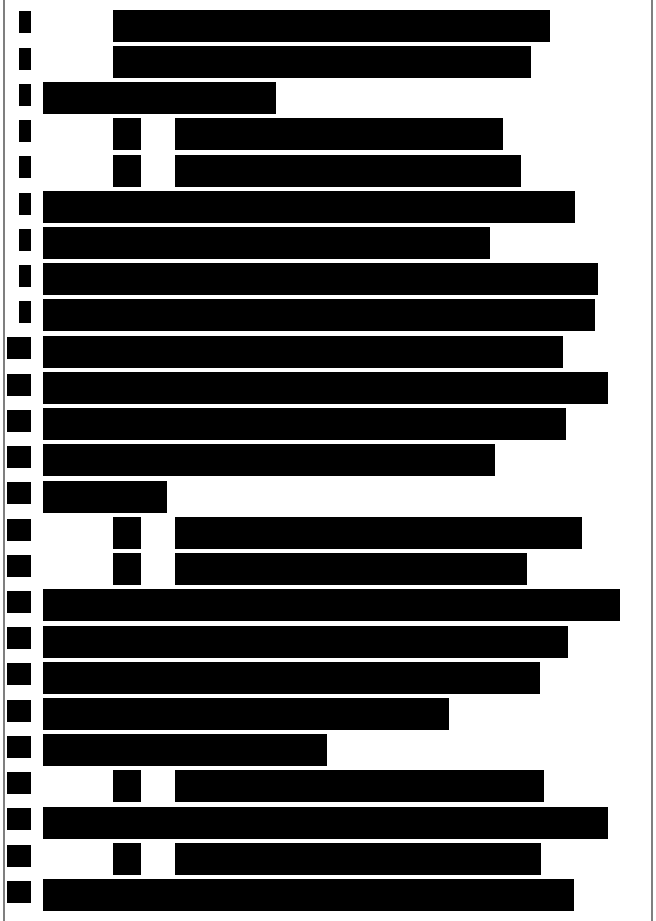

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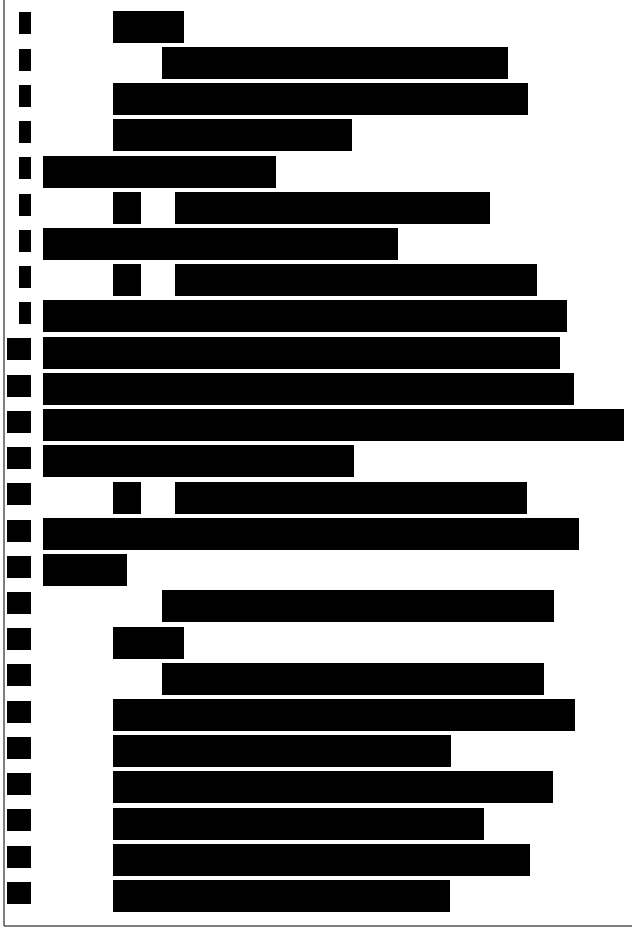

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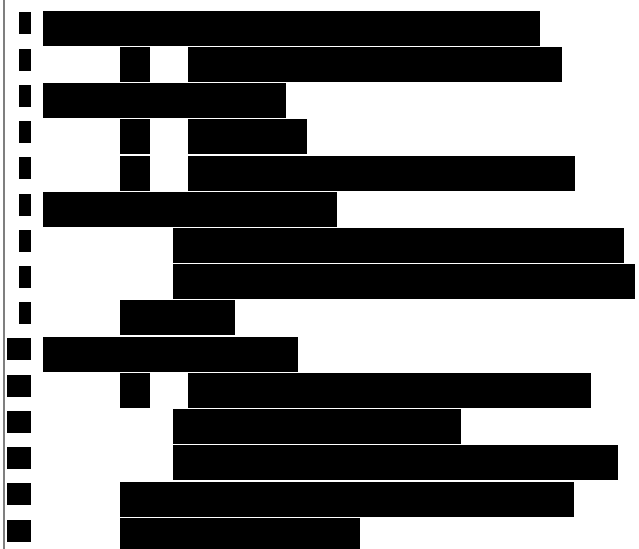

MR. VAUGHN: All right, Melisha, let's go to EMA Press Release regarding GVK Biosciences.

This will be Exhibit 31.

(Exhibit 31 was marked.)

MR. FOWLER: Let me just lodge an objection to the EMA exhibit having nothing to do with products sold in the U.S.; relevance and hearsay.

Go ahead.

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BY MR. VAUGHN:
Q. Doctor, have you ever seen this May 22nd, 2015 notice by the EMA?
A. No.
Q. Do you see where the EMA is suspending medications over flawed studies done by GVK Biosciences in India?
A. I do see that. I -- I also see later: "There's no evidence of harm or lack of effectiveness of any of the medicines linked to studies conducted by GVK."
Q. Were nitrosamines impurities in valsartan known in 2015?
A. I don't know.
Q. The third paragraph, do you see where EMA is discussing that GVK Biosciences manipulated data regarding generic medications over a period of the last five years?
MR. FOWLER: Objection to form, hearsay, lack of foundation, facts not in evidence.
THE WITNESS: Which page are we on?
BY MR. VAUGHN:
Q. On the first page, third

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Q. And GVK Biosciences was doing those bioequivalency tests for Defendants in this litigation over the time period referenced in this letter, correct? Over the last five years, as of 2015, e-mails; so between 2010 and 2015, correct?
MR. FOWLER: Objection: Form, foundation.
THE WITNESS: Yes. But, again, you know, they go on to say: "There's no evidence of harm or lack of effectiveness, and patients should continue to take their medicines as prescribed."

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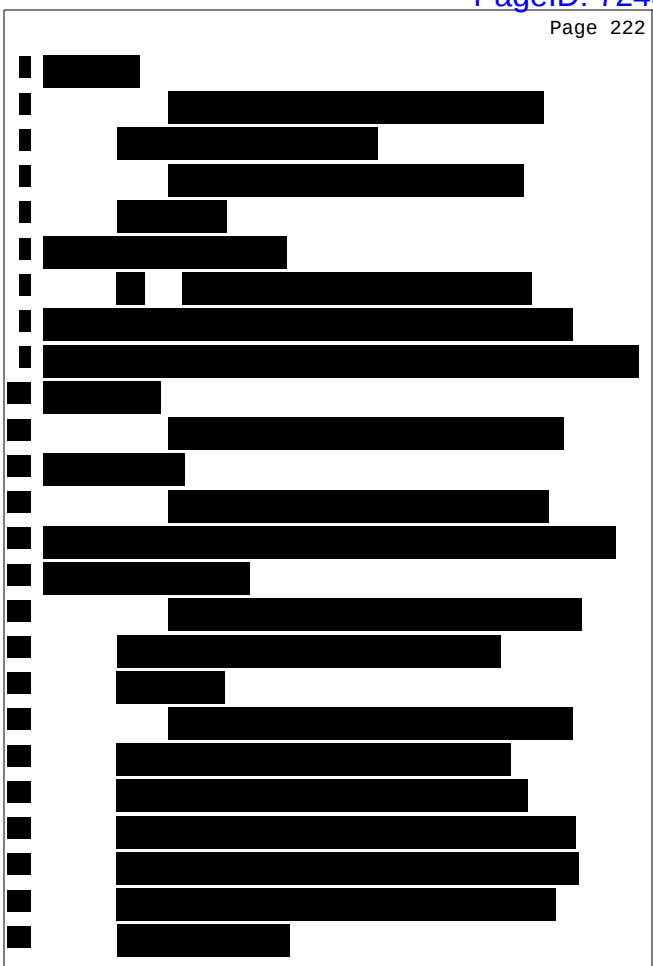

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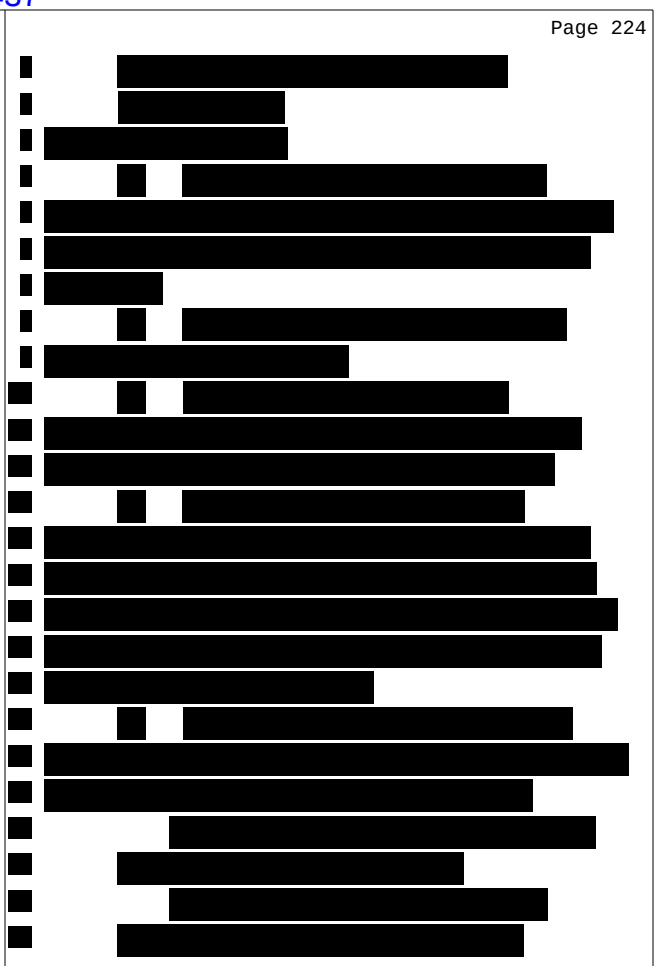

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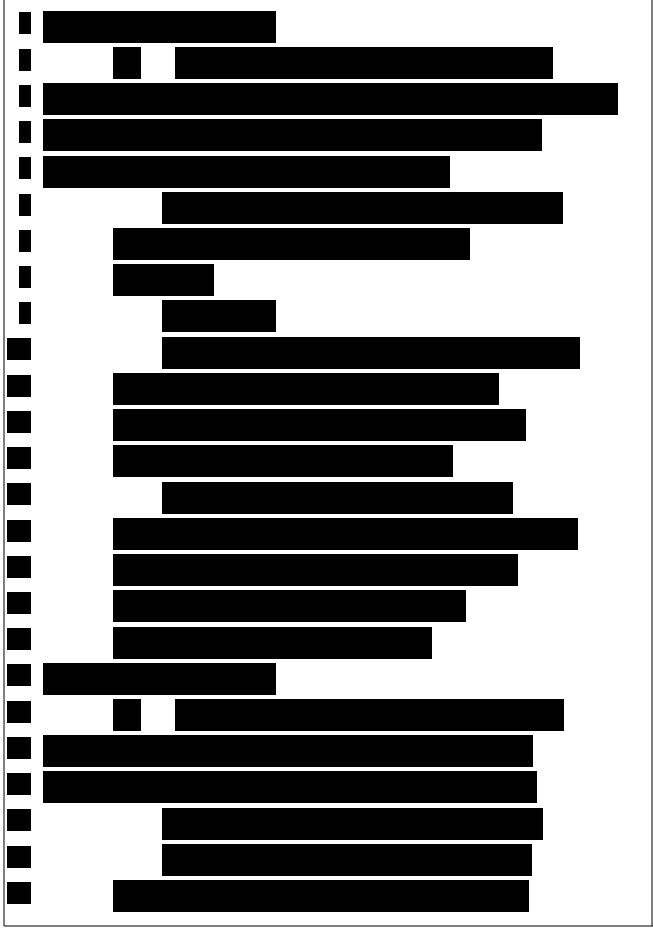

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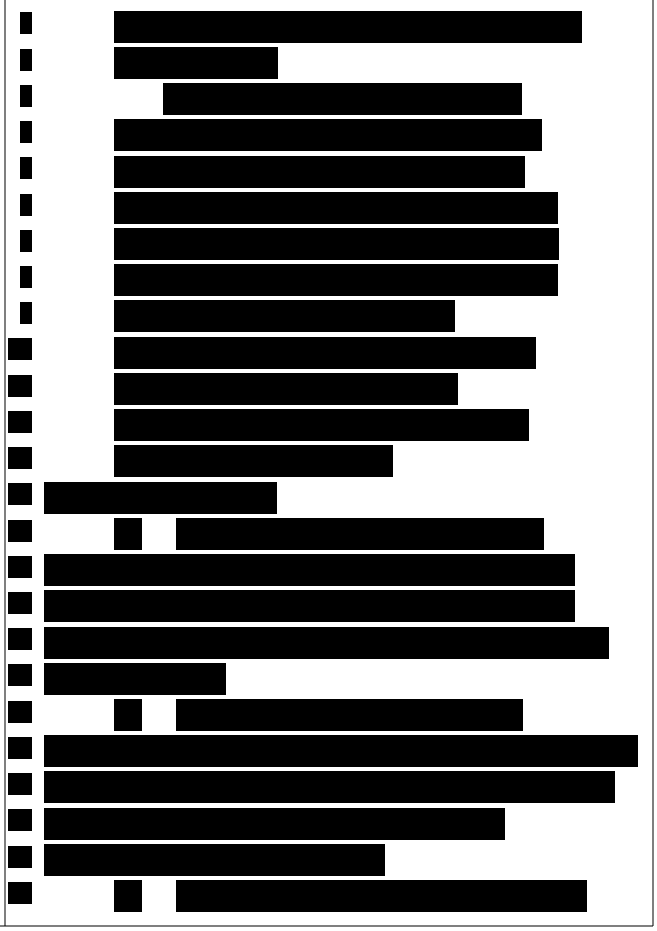

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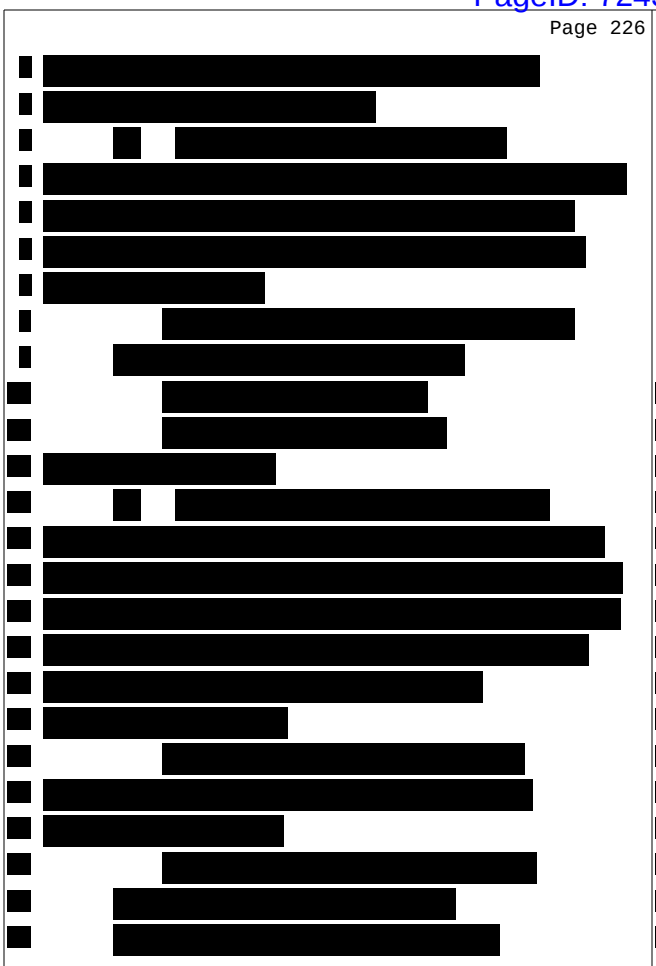

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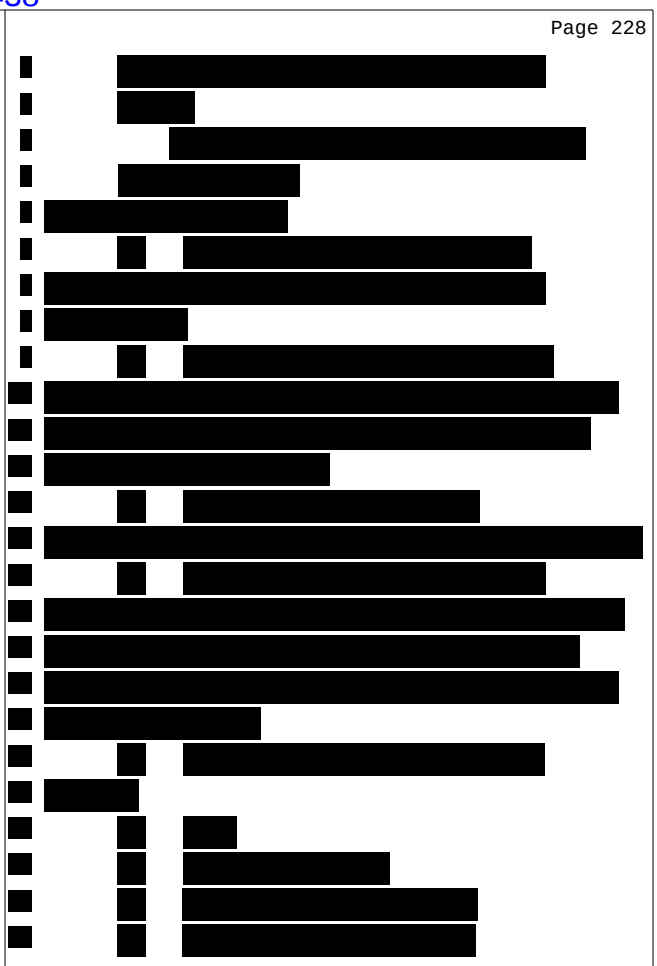

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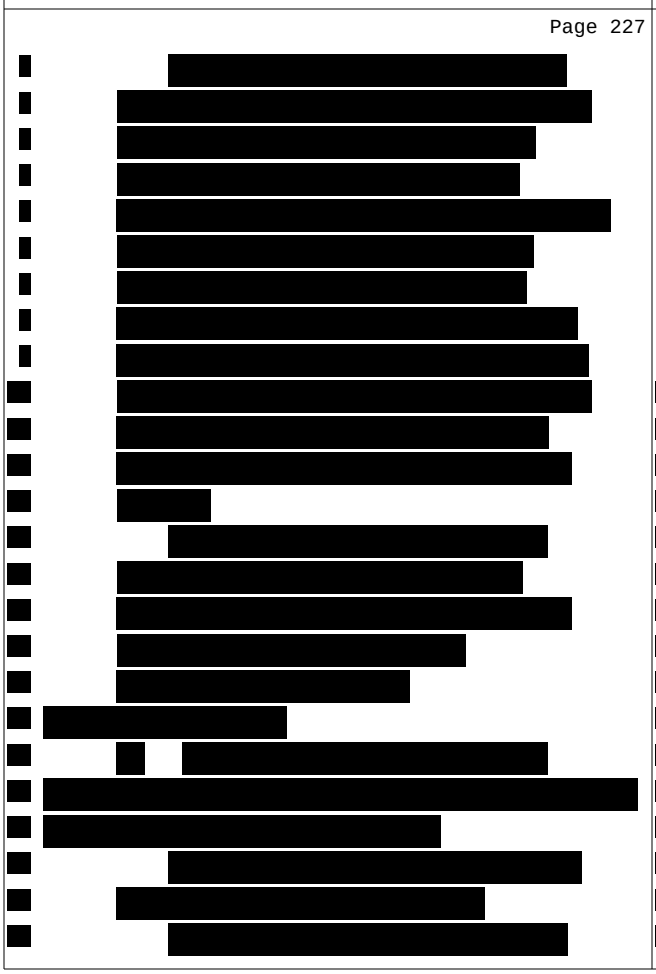

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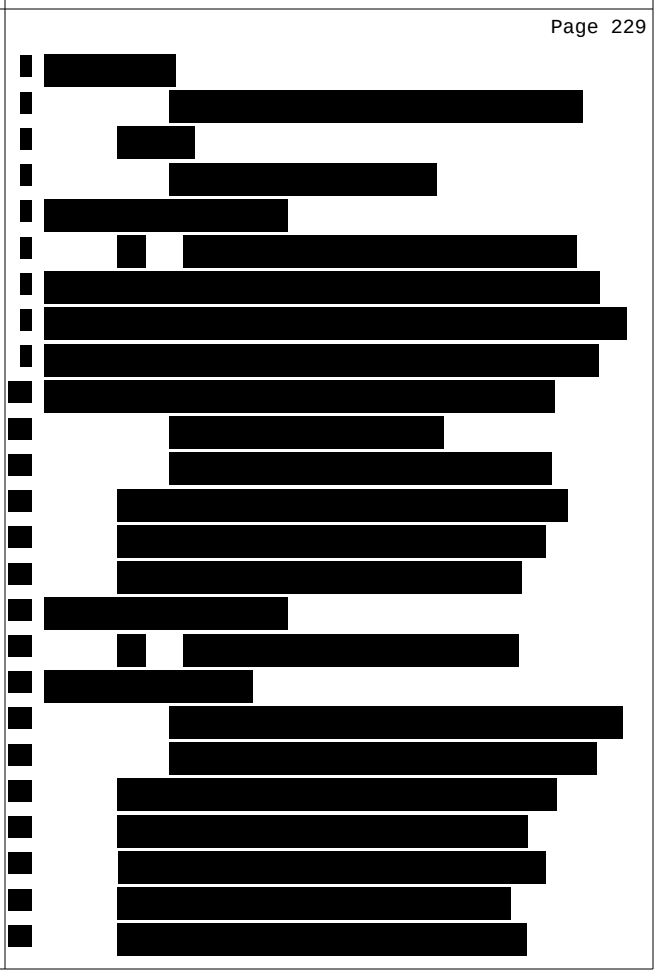

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[redacted]

MR. VAUGHN: All right. Melisha, let's pull up Bottorff 0001.

This will be Exhibit 33 [sic].

(Exhibit 34 was marked.)

THE VIDEOGRAPHER: 34, Counsel.

MR. VAUGHN: 34, thank you.

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BY MR. VAUGHN:

Q. Doctor, are the -- these the notes you took in preparation for your general causation expert report?

A. Yes.

MR. VAUGHN: Melisha, can we go to 11? All right, C? Do you see where that's at, Melisha? Yeah, paragraph.

BY MR. VAUGHN:

Q. Doctor, what does the last sentence of your notes say on that paragraph?

A. "New active ingredient does not equate to an int- -- contaminant." This is not my statement. These are -- in this section of my report, I was making notes on what was in the original filing. So it's a regurgitation of what someone else who filed the -- the causation lawsuit. This isn't me making a statement. It's me regurgitating what was put by someone else in the original lawsuit filed.

I even cite page 124, I think, in that paragraph just above. In the same paragraph, but just above there. So this isn't me. This is me quoting what was in the document I reviewed.

Q. Okay. And what about further

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down right below the very bottom where you note: "FDA inactive ingredients database does not involve contaminants which are covered under chemical hazards," is that from a complaint?

A. At this point, to put it into context, I was talking about the FDA definition of inactive versus an active ingredient, like I was referring to a few minutes ago, where the active ingredient is a drug product intended to furnish a pharmacologic activity in the diagnosis, cure, medication, treatment or prevention of disease.

Then there is an inactive ingredient database. And the FDA's inactive ingredient database are for things like excipients, methyl cellulose, mannitol, you know, things that are used in the tableting process. So that inactive ingredient database does not include contaminants. That's under Chemical Hazards in their database.

Q. And why are you taking notes on contaminants?

A. Because the section of the report or the original suit that was filed kept calling the -- the valsartan products unapproved because of the president [sic] -- presence of a

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contaminant. So I was making notes about what the FDA's definitions are in response to that portion of the filing.

Q. Is NDMA or NDEA chemical hazards?

A. I don't know if they're under the Chemical Database or not, but they're clearly considered an impurity.

Q. Are NDMA and NDEA chemicals?

A. Chemicals.

Q. What does the word "hazardous" mean to you?

A. Causing hazard.

Q. What does "hazard" mean to you?

A. Some form of hazard. It's a very broad definition.

Q. So it's your position -- go ahead.

A. I'm sorry. Just in my reports, I never disagreed with the IARC definition of NDMA, or NDEA for that matter, being a probable human carcinogen, which is exactly the category that they're listed in. I've never disagreed with that at all. What I've always contended in both reports, that it's an issue of how much and in what form of intake.

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Q. You don't disagree with the IARC definition that NDMA or NDEA are probable human carcinogens, but you dropped it from the second version of your expert report?
A. I dropped --
Q. Is it --
A. -- saying that I don't believe -- that I don't believe they are able to cause human carcinogenesis in the route of administration and at the doses or exposure levels that we're talking about.
Q. Is it -- in your opinion about the drugs -- that when drugs are approved but that they are contaminated -- scratch that.
Is it your position that a drug is only contaminated when it reaches an unsafe level of impurity or contaminant?
MR. FOWLER: Objection to form. You're outside the scope of the class certification report, Counsel. I'm letting this go a little bit, but you're -- you're far afield.
You need the question again, Doctor?
THE WITNESS: Yeah, if I'm

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expected to answer it, I would like to hear the question again.
MR. VAUGHN: Court Reporter?
THE COURT REPORTER: Yes?
MR. VAUGHN: I can reask it.
THE COURT REPORTER: It's okay. I can --
MR. FOWLER: We'll hear -- we'll hear it from the court reporter, please.
Go ahead.
THE COURT REPORTER: Okay.
(The previous question was read into the record as follows: "You don't disagree with the IARC definition that NDMA or NDEA are probable human carcinogens, but you dropped it from the second version of your expert report?")
THE WITNESS: And so, no, there was no intent by, quote/unquote, dropping it from my second report, which was implying that it was done intentionally, which it was not. So I still agree with the IARC classification of being probable human carcinogens. I have -- I have no reason to disagree

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with that.
My point is in humans, I don't believe they're carcinogenic in the manner in which they are taken, which is oral, at the levels of exposure, which are in the low microgram quantities.
BY MR. VAUGHN:
Q. And is it your position, then, that the contamination has to reach an unsafe level before it's actually considered a contamination?
MR. FOWLER: Objection, beyond the scope of this report, Counsel.
Can you make any proffer how that possibly relates to the class certification report that he has filed, or am I just missing something?
BY MR. VAUGHN:
Q. Doctor, do you think these drugs have any value?
A. What I believe, which is in the -- the rather lengthy Bioequivalence section of my report, is that the bioequivalence, due to the presence of NDEA or NDMA, is not altered and, therefore, they produce the intended therapeutic

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benefit, whether it was lowering blood pressure or managing heart failure or in a post-MI situation.
So, no, I don't believe they had any loss of their therapeutic benefit.
Q. Are you aware of it being illegal to sell a drug with an unsafe level of nitrosamines in them?
MR. FOWLER: Objection to form. By the very question, it called for a legal conclusion.
MR. VAUGHN: Please quit interrupting. You're -- you're coaching him. You've been coaching him the entire deposition.
MR. FOWLER: No, I'm not.
MR. VAUGHN: These are improper depositions. We're going to reserve our right for sanctions.
MR. FOWLER: So the Court has asked for specificity in objections, which I've provided, and it's a proper objection. Asking him if something is illegal asks for a legal conclusion.
MR. VAUGHN: Do you not recall the Court sanctioning you guys because

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you were objecting to "the document speaks for itself" previously, which has been one of your objections in this deposition? Do you recall that, Counselor?

MR. FOWLER: I'm not testifying, Counsel. Move on.

BY MR. VAUGHN:

Q. Doctor, are you aware that it would be illegal to sell a drug with unsafe levels of nitrosamines in them in the United States?

MR. FOWLER: Objection, form.

THE WITNESS: And -- and my answer is no, I do not have any opinion on what becomes legal or illegal. I have no legal opinions in this case.

BY MR. VAUGHN:

Q. If it would be illegal to sell something in the United States, does it really have any value?

MR. FOWLER: Form.

THE WITNESS: Again, I have no opinions on legality. My opinions were on whether the bioequivalence was violated by the presence of the

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impurities, and I do not believe that and I believe they maintain their therapeutic expected response.

BY MR. VAUGHN:

Q. Based purely off of bioequivalency studies that you reviewed that did not involve nitrosamines in the drug product?

A. I believe in answering that question a few times before, I said that there's a likelihood that some of the products did have nitrosamine in them. And if they did, it still wouldn't have affected their bioequivalence, and therefore their therapeutic response.

Q. And you have no document to cite to that they were likely contaminated at that time?

A. I have no document. I've -- I've previously stated that.

Q. Do you have an understanding of what it means for a drug to be adulterated?

MR. FOWLER: Objection: Form, outside the scope of this general -- this class action report.

THE WITNESS: I have a -- a basic understanding because of my pharmacy

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training and background, but my understanding of adulteration are impurities that are outside the manufacturing process, so during storage or some other nonmanufacturing process that results in adulteration.

BY MR. VAUGHN:

Q. Transportation of the drug product count, if it got contaminated during transportation?

A. I think that probably would fit under that adulterated category, because it's not part of the manufacturing process.

Q. And do you know if any of the Defendants are claiming that their product got contaminated during transportation?

A. Never seen such materials or documentation.

Q. Are you aware that if a drug is contaminated, it's considered adulterated?

MR. FOWLER: You're asking for a regulatory opinion. It's outside the scope of this report.

THE WITNESS: Yeah. Again, I -- I don't have regulatory input. That's

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-- that's not the nature of my report.

BY MR. VAUGHN:

Q. As a pharmacist, do you have an understanding that an adulterated drug is not supposed to be sold to U.S. consumers?

MR. FOWLER: Objection to form. Again, outside the scope of the class cert report and opinions therein.

THE WITNESS: Again, adulteration, I don't know is what we're talking about here, but pharmacists would not dispense a known adulterated product.

BY MR. VAUGHN:

Q. I have no further questions at this time.

MR. FOWLER: We'll take a few minutes, and I've got some redirect. Let's take ten.

THE VIDEOGRAPHER: The time is now 4:13 p.m. We're off the record.

(Brief recess observed.)

THE VIDEOGRAPHER: The time is 4:26 p.m. We're back on the record.

EXAMINATION

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BY MR. FOWLER:
Q. Dr. Bottorff, I'd like to show you what I'm marking as Bottorff Exhibit 35. And -- which is Defendants' Responses and Objections to Plaintiffs' Notice of Videotaped Oral Deposition Michael Bottorff, Pharm.D.
(Exhibit 35 was marked.)
BY MR. FOWLER:
Q. Handing you that. Have you seen that document before?
A. Yes.
Q. You've reviewed that with us?
A. I did.
Q. Okay. Let me mark as Exhibit 36 your Curriculum Vitae, Doctor.
(Exhibit 36 was marked.)
BY MR. FOWLER:
Q. Can you tell us whether that is your -- your current CV?
A. Yes.
MR. VAUGHN: Real quick, Counsel. Are these in the -- the folder for me to access?
MR. FOWLER: I believe so.
(Discussion off the record.)

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MR. FOWLER: Oh, I see what he's doing. Sorry, Counsel. I didn't understand my -- my colleague. He's -- he's load- -- loading those up.
BY MR. FOWLER:
Q. Is that -- continuing on 36, Doctor.
Does that CV include your more recent appointment to what you referred to as the IRB?
A. Yeah, the Advarra IRB is on here.
Q. Doctor, you were asked early on in the deposition about your experience with bioequivalency studies, and I believe you only got as far as maybe in your first year of residency at the University of Kentucky, or maybe undergrad.
Have you had other experience working with, conducting, bioequivalency studies?
A. Yeah. When I first started faculty at the University of Tennessee, that would have been 1983, I was probably involved in and analyzed and published maybe a dozen pharmacokinetic-based bioavailability studies with a variety of cardiovascular drugs. And so those are all publications that are -- that are in my

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CV. So it went -- it went beyond just me being involved in some bioequivalence studies in around 1982 or 1983, but probably the next ten years, I did maybe a dozen more of those kinds of studies.
Q. Doctor, do you recall some questions towards the end of -- of the questioning today with -- where you mentioned definitions of FDA concerning active ingredients and inactive ingredients.
Do you recall those questions?
A. I do.
Q. Let me mark Exhibit 37. This is 21 CFR 314.3 Definitions.
(Exhibit 37 was marked.)
BY MR. FOWLER:
Q. And if you'd take a look at that, Doctor, and I'd ask you: Does that document contain FDA's definitions of those active ingredient, inactive, things like that?
A. Yeah. This has -- I mean, it's the -- it's the Code of Federal Regulations 314, so they're in here.
Q. Can you locate the Active Ingredient definition and read it for the record, please?

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A. Let's see. "Active ingredient is any component that is intended to furnish pharmacologic activities or other direct effect of the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure of function of the body in man or -- or animals," if it's veterinary products.
"The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect."
So it's an intended act or ingredient.
Q. Thank you.
And can you read Inactive Ingredient, please?
MR. VAUGHN: Steve? Steve, I'm still not seeing this document in the exhibit folder. I've refreshed it several times.
MR. FOWLER: Tim's working vigorously.
MR. VAUGHN: He's working on dropping it in, is that what you said?

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MR. FOWLER: Yeah. He's working on it. I threw him a curve ball. Sorry.
MR. VAUGHN: All right.
MR. FOWLER: He wasn't ready for that one.
MR. VAUGHN: Not a problem.
BY MR. FOWLER:
Q. Doctor, can you find the definition of Inactive Ingredient in that CFR document?
A. Yes. That's on page --
Q. They're alphabetical, aren't they?
A. Yeah. That's on page 5 of 11 in that document. It's any component other than the active ingredient.
Q. Is that what it says?
A. That's what it --
Q. Can you read it verbatim?
A. "Inactive ingredient is any component other than active ingredient."
So that would cover contaminants, impurities, excipients, or whatever.
Q. It refers to specifically the

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components, doesn't it?
A. Yes.
Q. Can you read the definition for a Component?
MR. VAUGHN: May the record reflect as the Defense counsel repeatedly objected to any type of regulatory questions or opinions and now is solely focussed on regulatory questions.
THE WITNESS: "Component is any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug product."
So that could be a lot of excipients and those kinds of things.
BY MR. FOWLER:
Q. Thank you.
Doctor, have you seen anything in the documents that -- that Plaintiffs' counsel has shown you today with regard to the ANDAs or the bioavailability studies that change -- change any of your opinions in this case?
A. No. And -- and I don't think

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it's uncommon when companies are making generic products, sometimes on the first run, to have something that ends up not being bioequivalent and requires going back to the drawing board and altering particle size or some other component of the formulation until they -- until they get the product that is going to be bioequivalent that would then be FDA approved, the ANDAs approved, and then it's allowed to be given to patients as an AB-rated generic drug.
That's not, I don't believe, uncommon. I don't have statistics on that, but I think it's unrealistic to expect them to get it right on the first time every single time. And those are -- as long as those are disclosed to the FDA that we made this change and now we want this approved, and then the FDA approves it. And so all the ANDAs that I -- I included in my report were FDA reviewed, approved, AB-rated and allowed to be generically substituted for a brand name valsartan product.
Q. Did any of the BE documents, even including the failed ones that counsel showed you, did any of those show that the valsartan's bioequivalence was affected by the presence of

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other compounds, whether they be, you know, amlodipine, HCTZ or the combination thereof?
A. Yeah, again, we don't know which did or didn't have NDMA, but inclusion of the combination products was demonstrated to support a scientific conclusion that without an overlapping either metabolism or drug distribution system, that those compounds in with valsartan, even in milligram quantities, much less microgram quantities, would not be expected to have any altering effect on the bioequivalence, and therefore the therapeutic response to valsartan.
Q. Regard to -- I'm showing you what was marked as Exhibit 19. This, I'll refer to it as the bankruptcy document with regard to PRACS. Is there any mention of valsartan or valsartan testing anywhere in that document?
A. No.
Q. With regard to the -- with regard to Exhibit 20, Doctor, do you recall the -- the questions concerning Cetero's bioequivalence data and FDA's investigation of that?
I'm showing you 20 -- Exhibit 20. Do you recall those questions, the questions on the document?

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A. Yes.
Q. Can you turn to the second page and identify what are the drugs that those ANDAs of reference in that Exhibit 20, what are those drugs?
A. Federal Register Notices on October 28th. "The agency is proposing to withdraw Watson's Oxycodone/ibuprofen ANDA and InvaGen's Trandologril (phonetic) ANDA."
Q. Is there anything in that document that suggests FDA was critical of any testing of the valsartan bioequivalence, if any was done at all at that -- by that company at that location?
A. No mention of valsartan at all.
Q. Doctor, can you explain why it is that you spent the time reviewing the BE data from each of the various generic manufacturers for the various drugs, whether it's valsartan by itself or in combination? What was the im- -- what was the importance? What was -- why did you review those -- that data, and how did it factor into your opinion?
MR. VAUGHN: Object to the form.
THE WITNESS: Again, from a pure

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scientific standpoint, if two compounds that are known to be in the same tablet, let's say, have the chance to interfere with each other altering the effect of certainly the intended compound, in this case valsartan, then I wrote a -- a fairly lengthy section in my report about what are the different mechanisms whereby there would be an interruption of the valsartan effectiveness. It had to be its absorption, it had to be its metabolism, it had to be its hepatic distribution, or its effect at the angiotensin II receptor site.
And there's no mechanism whereby NDMA or NDEA can do that. There's no mechanism whereby hydrochlorothiazide, which is in there, can do that. And there is no mechanism where amlodipine does that. So none of those substances have any mechanisms to alter either the kinetics or the therapeutic response to valsartan.
BY MR. FOWLER:
Q. You were shown -- let me, for

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example, hand you Exhibit 14 -- hand you Exhibit 14 (tendering) -- and direct your attention to the table showing the BE results.
Let me know when you're there.
A. I'm there.
Q. The BE results were outside of the 80 to -- is it 120 is the FDA range?
A. 125.
Q. When they are -- when the BE results as reflected there in Exhibit 14 were outside the range, do you attribute any of that to any presence of NDMA or NDEA?
A. No. Again, this is usually due to some type of tableting issue and -- and particle size. So it's -- it's -- I would not attribute it to NDEA or NDMA at all.
Q. Based on your understanding of the science of the bioequivalence study process, can you explain what reformulation does and how that would translate to different results of the BE studies?
MR. VAUGHN: Object to the form.
THE WITNESS: Yeah, again, this starts getting into a pharmaceutics process that's a little bit -- I've had

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a little bit of training in that and -- and understanding and have read some articles throughout the years.
But it's mostly involving the -- the tableting, the particle size, the pressure with which you compress the tablet, the film coating, the things that result in the tablet disintegrating and then releasing the active ingredient.
And so it's -- it's more of a pharmaceutics development, tinkering that you do with your products to get the intended dissolution and then ultimate bioequivalence that you're looking for.
BY MR. FOWLER:
Q. Does the fact that some of the studies, the BE studies you were shown by counsel, were studies under 100 percent males and 100 percent Asian males, does that have any impact on -- first of all, on the validity of the BE results?
A. No. Again, the FDA allowed those studies to be done and approves the ANDAs in the

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face of those. And remember, what you're doing with the bioequivalence study in the same person is comparing test product with reference products.

And then you take it to another person and you test, test product versus reference product. And the fact that that, both times, was in a male or that they weighed 60 kilograms, if you then take that same release characteristic to a female or a person that weighs 78 kilos or a person that's 39 instead of 29, you're still within that same person going to see the -- the approvable release characteristics in that -- between those two products. It'll retain its bioequivalence.

Q. Do the test subjects or the test methodology of the BE studies, that you were shown, impact your opinion with regard to the presence of NDMA and its impact, if any, on bioequivalence?

A. I think it's --

MR. VAUGHN: Object to form.

THE WITNESS: -- a similar question worded slightly -- I'm sorry, go ahead.

MR. VAUGHN: I -- object to form.

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You're good.

THE WITNESS: Okay. I think it's a similar question asked a slightly different way, and -- and as I've stated multiple times today -- and it's in my report -- the presence of NDMA and NDEA, there's no mechanism, no scientific rationale beyond how they could alter the bioequivalence of any of the valsartan products.

BY MR. FOWLER:

Q. Would that be true for either gender or any race, in your opinion?

A. Yeah, that's -- would be independent of those issues.

Q. Early in the deposition, there were questions about the circulation of -- of blood.

Do you recall those questions?

A. Uh-huh. Yes. Sorry.

Q. And does -- how, if at all, does the blood circulation play a role in your opinions in this case with regard to the NDMA and -- and the valsartan?

MR. VAUGHN: Object to form.

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THE WITNESS: In -- in the context that we were talking about at that time, we were talking about the ability to measure an elimination half-life and how that's affected by blood flow, liver blood flow. You can only measure that if there's drug in the blood. And with NDMA at the amounts that we're talking about, that has to be given intravenously, and then you can measure the decline in blood because it started there and you watch it go down. And some of that blood flow goes to the liver, some goes to the heart, some goes to the lungs, you know, whatever.

That issue doesn't apply when you talk about giving low doses of these high-clearance drugs in an oral format that don't reach the systemic circulation. You can't measure a half-life in a situation where there's no measurable drug there to begin with.

BY MR. FOWLER:

Q. Doctor, directing your attention to your report. Do you have that in front of you?

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A. I do.

Q. Has counsel asked you about all of your opinions in your report today?

A. Pretty much focussed on -- on bioequivalence, I would say.

Q. Do you have -- turning your attention to page 52. Do you see a Summary of Opinions and Conclusions section?

A. Yes.

Q. Would you please read both of those points on page 52 going over to 53 to the third point, please?

A. Okay. There are three main points that I addressed in -- in my report, and they're -- they're summarized on the end of page 52 and at the beginning of page 53.

The first is relevant to what we had a lot of questions on today, and it basically is that the presence of NDMA and NDEA in valsartan could not have had any effect on the kinetics, dynamics, bioavailability or bioequivalence of valsartan generic products because there's --

Q. Just please -- just read your -- read from your paragraph, please.

A. Oh, read it verbatim?

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Q. Yes, sir.
A. I'm sorry.
Q. You were doing fine.
A. "The compounds do not share any known pharmacokinetic or pharmacodynamic mechanism. The presence of active intended ingredients with valsartan, such as hydrochlorothiazide or amlodipine, also did not alter valsartan bioequivalence for the same reasons, so there is no overlapping pharmacokinetic process. Thus, there is no conceivable way for NDMA or NDEA, merely by being present, to alter the bioequivalence of valsartan, and thus its therapeutic response and efficacy."
Q. Thank you. And you have another opinion?
A. And my second opinion gets back to this concept of first pass metabolism. "The levels of NDMA or NDEA that the FDA has detected in affected valsartan tablets, when these are taken on a daily basis, would not exceed the liver's capacity to metabolize the NDMA or the NDEA contained in those tablets in a first pass metabolism process. And according-" -- "accordingly, NDMA or NDEA is unlikely to reach

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the systemic circulation or other organ systems outside of the liver; therefore, there is no scientific basis to assume that there is any increased risk to other organ systems which support the medical monitoring that is proposed by Plaintiffs' expert Dr. Kaplan."
Q. Thank you.
And on the -- on the next page, do you have another opinion?
A. I have another opinion, and -- and this was more of a mathematical. "Based on the known pharmacokinetic principles of accumulation, the daily exposure" -- which in this case is usually every 24 hours -- "to NDMA or NDEA would not accumulate, given the known elimination half-life of these compounds, which are in" -- "measured in minutes."
So to give something that's gone in three to five half-lives, of a five- to ten-minute elimination rate, there's no way, given that once every 24 hours, could lead to any type of accumulation at all.
Q. Do you hold those opinions to a reasonable degree of medical -- of scientific certainty?

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A. Yes.
Q. We also marked --
MR. FOWLER: I think we're up to Exhibit 37 [sic], Counsel.
BY MR. FOWLER:
Q. -- simply the list of materials considered that was provided to you. I just wanted to mark that as an exhibit.
(Exhibit 38 was marked.)
BY MR. FOWLER:
Q. Doctor, do you recognize that as your Materials Considered list?
A. Yes.
Q. And then Exhibit 38 [sic] is --
MR. FOWLER: Counsel, I'm holding up the flash drive of Dr. Bottorff's Materials Considered. So we're going to send this to the court reporter as we've done in other depositions and be copied that way.
This is Exhibit 38 [sic]. Madam Court Reporter, we'll mail that to you.
(Late-filed Exhibit 39 was marked.)
BY MR. FOWLER:

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Q. If you'll indulge us for a moment, I may be about finished.
My much more attentive colleague has pointed out that the Materials Considered is 38 and the flash drive should be 39, so we'll just fix that.
And with that, I'll -- I'll -- I have no further questions.
Thank you very much, Doctor.
MR. FOWLER: Counsel.
MR. VAUGHN: Can you just give me five minutes to consult with my cocounsel? I'll be right back. We'll be real quick.
THE VIDEOGRAPHER: Shall we go off the record?
MR. VAUGHN: Please.
THE VIDEOGRAPHER: The time is 4:51 p.m. We're off the record.
(Brief recess observed.)
THE VIDEOGRAPHER: 4:56 p.m., we're back on the record.
EXAMINATION
BY MR. VAUGHN:
Q. Dr. Bottorff, do all of your

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opinions contained within your class action expert report apply equally to all potential class members?
A. I'm not sure exactly what that question means. What -- what -- what does that mean exactly so I can better answer it?
Q. Which part of the question are you having trouble with?
A. Well, maybe start with the definition of the class members. Are they the people who have filed, like, claims or....
Q. I -- I understand now, Doctor.
Do all of your opinions contained within your class action expert report apply equally to all of the Defendants?
A. Again, I don't know if I had bioequivalence data on -- well, from every Defendant, but I -- I think it does because of the reasons behind it. It doesn't matter that NDMA may have been in there or not. It wouldn't affect the bioequivalence. So I guess I would say yes.
Q. As a pharmacist, if you are in possession of an adulterated drug, would you return that adulterated drug to a manufacturer, or would you just throw it away?

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MR. FOWLER: Objection: Form, scope.
THE WITNESS: I've never been in that position of -- in -- in that type of practice. I guess I would follow whatever my -- my company's policy was. But I don't -- I don't know what that is. I don't know what that would be.
BY MR. VAUGHN:
Q. Would you be afraid of contaminating the groundwater if you're just throwing away drugs that are contaminated with carcinogens?
MR. FOWLER: Objection, outside the scope of my redirect completely.
MR. VAUGHN: Your redirect had him answer quest- -- testifying on every single one of his opinions. You completely opened the scope up.
THE WITNESS: Well, what I can answer is that that's not how in pharmacies that we get rid of drugs anymore. There are drug take-back programs that almost every pharmacy runs periodically, and there's some

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destruction process that is not flushing them down the toilet. So that's just not how it happens these days.
BY MR. VAUGHN:
Q. All right. Regardless, you wouldn't be able to sell the contaminated drugs, correct?
MR. FOWLER: Objection: Form, outside the scope of his report and his testimony and the redirect.
THE WITNESS: Yeah, I -- again, in -- in your hypothetical, you would have to know that something was adulterated, so I don't -- I don't know what that process is.
BY MR. VAUGHN:
Q. As a pharmacist, if the FDA would not let you sell a drug to the U.S. public, what would you do? Would you be able to get your money back from the manufacturer?
MR. FOWLER: Objection, form.
This is outside the scope of his entire report, of his testimony, and outside of my redirect. Nothing about The redirect opened up questions for

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what a pharmacist is going to sell, Counsel.
MR. VAUGHN: He -- he submitted an expert report in a class action saying this stuff is worth money.
MR. FOWLER: You should have asked him about that in your case in chief here on -- on direct. You're going back, for whatever reason. It's outside the scope, and I would have objected to it in the first place.
MR. VAUGHN: You did object to it a bunch in the first place and then you were coaching the witness before and then you opened everything back up by having him read every one of his opinions. You opened the scope.
MR. FOWLER: I'm not going to argue with you, Counsel. The words "sell the drugs" was nowhere in his opinions.
BY MR. FOWLER:
Q. If you can't sell a drug --
(Unintelligible overlapping.)
BY MR. VAUGHN:

Q. -- Doctor, does it have any value?

MR. FOWLER: I'm sorry, I spoke over you, Counsel. Please state that again.

THE WITNESS: Or I -- I never answered the previous question.

MR. FOWLER: He withdrew.

THE WITNESS: Oh, okay.

MR. FOWLER: So a new question. Go ahead.

BY MR. VAUGHN:

Q. Would you like to answer the previous -- would you like to answer the previous question, Doctor?

A. If you would like me to.

Q. So as a pharmacist, if the FDA will not allow you to sell a drug to the U.S. public, would you be able to get your money back from the manufacturer?

MR. FOWLER: Same objection.

THE WITNESS: And I would say that I've never been in the situation to understand how that works. That's not my -- my academic career has been

working in hospitals with cardiology patients and cardiologists, and I've never worked in that environment, so I -- I had no experience with that at all.

BY MR. VAUGHN:

Q. If you can't sell the drug, Doctor, does the drug have any value?

MR. FOWLER: Form, incomprehensible.

THE WITNESS: Again, I -- I mean, in a hypothetical, if you can't sell it, then obviously you can't sell it, so....

BY MR. VAUGHN:

Q. Absolutely.

A. So I would say, yeah, if you can't sell it -- so it doesn't have value if you can't sell it.

MR. VAUGHN: I have no further questions.

MR. FOWLER: He'll read.

MR. VAUGHN: Thanks for your time again, Dr. Bottorff.

MR. FOWLER: Nothing further.

THE VIDEOGRAPHER: The time is 5:02 p.m. This concludes today's

testimony from Dr. Michael Bottorff.

We are now off the record.

FURTHER DEPONENT SAITH NOT.

(Proceedings concluded at 4:02 p.m. Eastern.)

REPORTER'S CERTIFICATE

I certify that the witness in the foregoing deposition, MICHAEL BOTTORFF, PHARM.D., was by me duly sworn to testify in the within entitled cause; that the said deposition was taken at the time and place therein named; that the testimony of said witness was reported by me, a Shorthand Reporter and Notary Public of the State of Tennessee authorized to administer oaths and affirmations, and said testimony, Pages 7 through 258 thereafter transcribed into typewriting.

I further certify that I am not of counsel or attorney for either or any of the parties to said deposition, nor in any way interested in the outcome of the cause named in said deposition.

IN WITNESS WHEREOF, I have hereunto set my hand this 4th day of April 2022.

_____

Carissa L. Boone, LCR No. 382

My License Expires: 6/30/2022

E R R A T A

I, MICHAEL BOTTORFF, PHARM.D., having read the foregoing deposition, Pages 7 through 268, taken March 25, 2022, do hereby certify said testimony is a true and accurate transcript, with the following changes (if any):

PAGE	LINE	CHANGE	REASON
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MICHAEL BOTTORFF, PHARM.D.

_____
Notary Public

My Commission Expires: _____